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III. *Bleeding from Special Sites*

A. **ADENOID FOSSA.** Severe hemorrhage following adenoidectomy can usually be controlled by insertion of a posterior nasal pack. For technique see Topic 73 (II-H).

B. **EARS.** If traumatic, this is pathognomonic of skull fracture [Topic 54 (VII-B-2-a)] provided there are no lacerations of the external auditory canal.

TREATMENT. Hospitalize *at once* for head injury care. A sterile pad may be applied over the ear, but nothing should be inserted. No attempt should be made to cleanse the canal.

C. **INTRACRANIAL**

1. EXTRADURAL (Epidural). Caused by the tearing of the middle meningeal artery or its branches with collection of blood between the dura mater and the skull. Direct trauma is the usual cause—persons between 20 and 50 represent the majority of cases.

SIGNS AND SYMPTOMS

...ory of trauma—sometimes very slight—to the head.
...idence of a fracture line crossing the groove for

Poisons

—A—

ACETANILID (Acetophenetidin, Aminopyrine, Antipyrine, Headache Powders, Phenacetin, Pyramidon, Coal Tar or Aniline Dyes)

SYMPTOMS

1. Nausea and vomiting.
2. Cyanosis, especially of the face.
3. Cold clammy skin.
4. Feeble pulse, slow respiration.

TREATMENT

1. Universal antidote
2. Emetics.
3. Gastric lavage with 1 pint (500 cc.) of 1:2000 ganate solution.
4. External heat.
5. Caffeine sodiobenzoate gr. 7-1/2
6. Oxygen or Carbogen ther...

4

the attending physician, together with his impression as to the cause of death.

4 DRUG DOSAGE IN CHILDREN

The following dosage table has been found satisfactory for emergency use:

AGE	COMPARISON WITH ADULT DOSE	AGE	COMPARISON WITH ADULT DOSE
...th	1/20	3 years	1/5
		4 years	1/4
		... years	1/3

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CARDIAC ARREST

Brian Blades, M.D., Washington, D. C.

Recent medical literature contains numerous accounts of cardiac standstill occurring during the induction of an anesthetic or while a surgical operation is in progress. Newspaper descriptions of this tragedy and treatment by massaging the heart have, in particular, made the public aware of this tragic complication. The terrifying possibility of the heart stopping has entered the minds of many who require surgical operations and in fact has caused patients to decline necessary and probably life-saving procedures. It is of the highest importance that the prevention, diagnosis, and treatment of cardiac arrest be understood by the medical profession, but it is of equal importance to stress the relative infrequency of this complication when its incidence is compared with the enormous number of surgical operations done each year.

This does not imply the importance of cardiac arrest should be minimized, nor does it mean that the extensive educational program led by the magnificent work of Claude Beck and others should not continue with even more vigor. The ideal goal is no cardiac arrests. Until this can be achieved, it would be comforting if, when the catastrophe does occur, one could honestly know in retrospect that no error of omission or commission could be found to account for it and that proper and prompt treatment had been given.

Accumulated data from various clinics and studies of large series of anesthetics and operations suggest that a fair average figure for the incidence of cardiac arrest might be one in 5,000 cases. Bonica [1] recorded 13 cases of cardiac arrest in a five year period that included 64,400 cases on surgical and obstetric services. This incidence corresponds roughly with the observations of Lahey and Ruzicka.[2] At the George Washington University Hospital only two cardiac arrests occurred in 42,636 operations in the period between 1948 and 1952. There were none in about 7,000 operations in 1953. Precise evaluation of the number of cases in which true cardiac arrest develops is difficult, because in all types of sudden death the heart eventually stops. It would seem safe to assume that in some cases sudden cessation of the heartbeat in the operating room or during induction of anesthesia results from coronary occlusions, pulmonary emboli, or other factors and that these are not true examples of sudden cessation of cardiac function from the effects of anesthesia or surgical manipulation.

PREVENTION OF CARDIAC ARREST

Successful prevention of cardiac arrest requires knowledge of the physiological principles involved. Anoxemia is the common denominator. Lack of available oxygen for the myocardium may be the result of either impaired ventilation or impaired circulation. Impaired ventilation leads to anoxia, anoxemia, myocardial anoxia, and, finally, fibrillation of the ventricles, which may lead to cardiac standstill and death. The same mechanism prevails if the circulation is inadequate to provide oxygen to the myocardium.

Impaired Ventilation.—Inadequate ventilation may result from mechanical or chemical factors. Any obstruction of the airways—whether it be from a poorly placed intratracheal catheter, a tumor, or from accumulated mucus or blood—decreases pulmonary ventilation; this in time will be reflected in respiratory exchange and will lead to anoxia. The same effect will follow if insufficient oxygen concentration is used with an anesthetic agent of the inhalation variety. The principal chemical factors in impaired ventilation and respiration are the result of the misuse of premedication drugs in addition to or supplanting the anesthetic agent whether inhalation anesthesia or local drugs are employed.

In this connection I should like to quote a portion of Dr. Robert S. Dinsmore's discussion of a paper on the surgical treatment of ventricular fibrillation by Johnson and Kirby [3]: "First of all the patient is met in the operating room by a man with a scalpel and another fellow with a machine with everything on it but a sledge hammer, which he does not need for he has done it with drugs and agents. The patient may be given multiple barbiturates early in the morning followed by morphine then by atropine, then by a little bit of pentothal induction and, actually, it is easier to place an intratracheal tube in if we use a little cocaine. Then you give the patient some nitrous oxide, some ether, or some cyclopropane and after all this you are allowed to put on the drapes. Then

From the Department of Surgery, George Washington University School of Medicine.
1. Bonica, J.: Role of Anesthesiologist in Management of Cardiac Arrest, Current Res. in Anesth. & Analg. **31**: 1, 1952.
2. Lahey, F. H., and Ruzicka, E. R.: Experiences with Cardiac Arrest, Surg., Gynec. & Obst. **90**: 108, 1950.
3. Johnson, J., and Kirby, C. K.: Surgical Treatment of Ventricular Fibrillation, Ann. Surg. **134**: 672, 1951.

you start to operate and the abdominal wall is rigid and the surgeon becomes rigid and the anesthetist limp. Then you give some curare. You cannot tell me that all those drugs and agents are not the factors. You simply add up to a multiplicity of drugs and too deep anesthesia."

All anesthetic agents are insidious poisons, if mishandled. It is probably not so much the agent but how the agent is employed that counts. Three factors must be considered in the use of anesthetic agents—the patient's comfort, the proper anesthetic to allow the technical job to be done properly, and, finally, the patient's safety. The final factor must have priority. Most general anesthetics cause hypoxia (respiratory depression) or coronary ischemia (vasomotor depression). Hypoxia sensitizes the heart, increases the circulation of epinephrine, and sensitizes the carotid sinus to inhibit cardiac activity. Specific agents such as chloroform, cyclopropane, and ethyl chloride sensitize the heart to circulating epinephrine and cause direct cardiac depression. Topical anesthetic agents such as cocaine and tetracaine (Pontocaine) hydrochloride are useful in the prevention of stimuli that would cause irritations in the pharynx, larynx, and trachea; these irritations may be laryngospasm or apnea, both of which lead to anoxemia. Contraindications to the use of these agents are individual sensitivity, which would cause respiratory or cardiac depression, and cerebral irritation due to absorption, which may cause convulsions. This latter effect may be counteracted by the administration of oxygen and thiopental (Pentothal) sodium. Laryngospasm may result from both mechanical and chemical factors. Circulatory collapse, coincident with the insertion of an intratracheal tube or manipulation of tissue, is sometimes contributed to a vasovagal reflex. Others believe that this is truly a manifestation of anoxia and not a nervous reflex mechanism. Nothing could be gained here by reviewing this controversial subject.

Failure to Maintain Circulation.—The maintenance of the circulation must be considered in terms of circulating blood volume and adequate oxygenation of the blood at all times. This is, of course, of particular importance during the performance of the operation and in patients who have alterations in blood volume or quality because of hemorrhage or other factors. The various fluids that can be administered intravenously and intravenous and, on rare occasions, arterial blood transfusions will usually furnish adequate protection. It is, however, unfortunate that there is not available a quick and easy way to determine blood volume. Another and sometimes neglected factor in the maintenance of circulating blood volume is the gentle handling of tissue.

PREOPERATIVE MEASURES TO PREVENT CARDIAC ARREST

It is possible that the availability of many valuable laboratory procedures has resulted in failure to appreciate the importance of a complete history and physical examination. The patient's recitation concerning his abilities in physical activities may be more important than reams of electrocardiographic tracings. If cardiac disease is known or suspected, exercise tolerance tests, electrocardiograms, and the possibility of specific medication in the form of such therapy as digitalis must be considered. It is significant that the incidence of cardiac arrest is no greater, if as great, in the so-called poor-risk patient than in the apparently good-risk patient undergoing an elective operation. This may suggest that all the precautions to prevent cardiac arrest are not exercised unless some abnormality in the specific case alerts the surgeon and anesthetist.

Preoperative medication is employed for specific reasons, and these reasons should be remembered. Drugs are used to decrease apprehension, produce a degree of amnesia, decrease reflex irritability, and lower metabolism. The easiest and surest method to produce cardiac arrest or ventricular fibrillation in the laboratory is the combination of anoxia and epinephrine. In the operating room it would appear that these principles would hold. The combination of a badly frightened patient, who has had inadequate preoperative medication and personal assurance, with a rapid induction with any anesthetic agent low in oxygen content should do the trick. This simple but essential point cannot be overemphasized. Considerable abuse has been directed at anesthesiologists in connection with the subject of cardiac arrest. Equal and severe criticism must be leveled at the surgeon who "toe-dances" about the operating theater demanding speed and a hurried induction of anesthesia so that he may get to the next case.

The principles of prevention of cardiac arrest during induction of anesthesia are simple. Too rapid induction with insufficient oxygen results inevitably in anoxemia and acapnia. An overdose of any anesthetic agent will produce respiratory depression or paralysis. An open airway and adequate oxygenation must be maintained.

POSTOPERATIVE PREVENTION OF CARDIAC ARREST

The patient should not be removed from the operating room until his condition is stable, the blood pressure and pulse are at satisfactory levels, and his color is good. He should be recovering from the anesthesia before leaving the operating room or the recovery room. The practice of hurrying to remove the patient who is supposedly dying from the operating room before death occurs is so wicked it hardly needs comment. The operating theater is by all odds the best place to attempt to save the patient who is presumed to be dying.

Postoperative suction of the airways must be observed in all patients, regardless of the type of operation or anesthetic employed. It is hardly necessary to offer a word of caution concerning the careful postoperative management of patients known to have cardiac disease. It is in these cases that the electrocardiogram should be employed frequently if the pulse is rapid or irregular so that a definite evaluation may be had of the arrhythmia or tachycardia. Overloading of the circulatory system with blood or fluids administered intravenously during or after surgical intervention must be avoided. This is particularly true in the patient with a deficient myocardium or pulmonary function.

TREATMENT OF CARDIAC ARREST

Before outlining the treatment of cardiac arrest, it is important to emphasize that attempts to resuscitate the heart without proper equipment and with inadequate knowledge of resuscitation are futile and account for a number of tragedies. It is difficult to know exactly when

the heart has stopped functioning as a pump. There can be no question that exploratory thoracotomy has been performed and cardiac compression carried out on hearts that were still beating with a certain, though limited, degree of efficiency. Condemnation of judgment and performance in these instances is not justified, and, conversely, any hesitation to act under these circumstances deserves the severest criticism. If the proper physical equipment is available, lives will not be lost by this maneuver, but a similar procedure without essential equipment can result in the death of the patient or the production of a pitiful, decerebrate human being.

Cardiac arrest may occur during anesthesia with any agent, local or general. The operation does not have to be of major proportions to cause cardiac arrest. The equipment listed below should be available in every operating room, whether the operations are of the so-called minor variety or the most serious. The necessary physical equipment consists of these things: (1) machines for artificial respiration, equipment and a supply of oxygen, and endotracheal tubes and face masks; (2) basic surgical instruments for a thoracotomy; (3) necessary drugs—procaine, epinephrine, and calcium chloride—syringes, and needles (it is important that there be duplicate sets of syringes and needles in case of breakage when the equipment is needed); and (4) an adequate defibrillator or electroshock apparatus. The defibrillator should be capable of delivering a 60 cycle alternating current of 110 to 220 volts, with 1 amp. or more of current flow since an amperage of below 0.8 amp. will cause fibrillation, and it should be equipped with a control switch that will operate at 0.5 sec.

The cardiac compression should be started within three minutes after cardiac arrest if the outcome of treatment is to be successful. There have been cases reported in which the delay was longer. These are difficult to evaluate since the exact level of circulation cannot be known and the only absolute method of diagnosis of cardiac arrest is observation of the heart. There must be, in the operating room, either the surgeon or one who is qualified to perform a thoracotomy and start cardiac massage. This procedure should be observed not only in patients with known heart disease or poor-risk patients but in all patients who are to be operated on.

Usage has injected the term "massage" as the maneuver employed in resuscitation of the heart. "Compression" is a better descriptive term, since the organ must be compressed vigorously to maintain a pumplike action sufficient to furnish oxygenated blood to the brain. Various opinions have been expressed concerning the number of strokes per minute that one should attempt in compressing the heart. It appears that as rapid compression as possible should be maintained. This is fatiguing work and a team of two or three with knowledge of cardiac resuscitation is necessary if the compression is to be maintained for any length of time.

The urgency of the situation may sometimes lead to neglect of the one absolutely essential measure: the patient must have oxygen. Artificial respiration by means of the anesthetic machine combined with the inhalation of pure oxygen should be instituted immediately. If an endotracheal tube is already in place, this problem is simple. If not, pure oxygen can be given with a tight-fitting face mask until an endotracheal tube is inserted. Attempts to undertake cardiac resuscitation without oxygen and the equipment to deliver it to the lungs deserve complete condemnation. Patients who otherwise might live because of a mistake in diagnosis can be put to death by suffocation and anoxemia when a thoracotomy is performed, or they might survive, but the very best that can be expected if there is a deficiency in oxygen intake is the production of a human vegetable.

Drug Therapy in Cardiac Arrest.—The drugs that are available for the treatment of cardiac arrest have specific actions and, if they are to be employed successfully, must be used only when their particular effect is desirable. The shotgun approach is worse than no drugs at all. Procaine should be used only to decrease myocardial irritability. If the heart is dilated and sluggish, procaine will aggravate the condition. The drug may be given intravenously in 10 cc. doses, 1% solution; by topical application on the heart, 1 to 2% solutions; or by intraventricular injections of 5 cc. of 2% solution. The second and most frequently misused drug is epinephrine. This agent must be employed with great caution and is extremely dangerous if the myocardium is cyanotic or fibrillating. Intravenous dosage should not exceed 1 cc. of a 1 to 10,000 solution. The same dosage may be used for intraventricular injections. The agent has its greatest value in the flaccid, sluggish heart. Calcium chloride may be used to increase myocardial tone and is a valuable drug for that purpose. A 5 cc. dose of a 1% solution given into the ventricle may be of great value.

Disappearance of a palpable pulse and audible blood pressure should be regarded as evidence of cardiac arrest or ventricular fibrillation. Differentiation of these two conditions before treatment is instituted would only be possible if an electrocardiograph happened to be attached to the patient at the time of the catastrophe. A delay to attempt to obtain electrocardiographic tracings in this situation would be stupid and disastrous. It is usually easy to determine whether the ventricles are fibrillating after the heart is exposed. The treatment of the two conditions is the same, namely, artificial respiration with pure oxygen and cardiac compression. Adequate compression will maintain circulation to the brain in either event. Once this is accomplished, there is no great hurry in applying electric shock for treatment of the fibrillation. If there is any doubt whether characteristic fibrillative twitchings are present, an electrocardiogram can be obtained.

Effective cardiac compression requires opening of the pericardium. Moreover, satisfactory inspection of the myocardium cannot be accomplished with the intact pericardium. During the performance of cardiac resuscitation, it is essential that the condition of the myocardium be noted. If the heart is dilated and cyanotic, further compression is required to improve its circulation and tone. This is true in both cardiac standstill and ventricular fibrillation. It is futile to apply electric shock to the fibrillating heart if it is cyanotic and deficient in blood.

SUMMARY

In both the prevention and treatment of cardiac arrest, adequate blood oxygenation and maintenance of circulating blood volume are the essential factors. It is possible that many instances of cardiac arrest could be prevented if proper precautions were maintained. The grave

consequences of the combination of anoxia and a high level of circulating epinephrine on cardiac function can be produced both in the operating room and the laboratory. The fearful patient subjected to a hurried induction of anesthesia or to too much anesthetic agent in the absence of oxygen may be expected to behave in the same manner as the laboratory animal who is partially suffocated deliberately and at the same time given epinephrine experimentally to produce ventricular fibrillation or cardiac standstill.

It is safe to predict that the extensive teaching program on the prophylaxis and treatment of cardiac arrest will reduce its incidence. It is of prime importance that the relative infrequency of this complication and the educational program of prevention and treatment be known to the public so that necessary operations will not be refused by patients terrified by newspaper accounts.

ADDENDUM

Since the preparation of this paper, two additional instances of cardiac arrest have occurred at this hospital, making a total of four cardiac arrests in 54,579 operations. In each case the treatment was instituted promptly. Two patients died; the other two recovered completely.

FREQUENCY AND SIGNIFICANCE OF BLEEDING IN EARLY PREGNANCY

Harold Speert, M.D.
and
Alan F. Guttmacher, M.D., New York

Bleeding from the genital tract is an invariable concomitant of reproduction in many species of vertebrates. Most familiar is the macroscopic blood loss that occurs after parturition in mammals with deciduate placentas. Less well known is the microscopic bleeding of maternal origin that accompanies the early stages of placentation and embryonic development. It is the purpose of this paper to summarize the evidence for this phenomenon based on observations in other species and to present evidence for its occurrence in man.

BLEEDING IN LOWER VERTEBRATES

Throughout the vertebrate subphylum, whenever the embryo is dependent on maternal sustenance beyond the ovum stage, red blood cells may be found in admixture with the pabulum of the brood chamber. In a delightful little essay on the phylogeny of menstruation, Carl Hartman [1] called attention almost a quarter of a century ago to the purposeful nature of this maternal bleeding, even as it occurs in the viviparous fishes and Amphibia. In certain salamanders, for example, the one or two embryos that survive from among the large number of ova shed at ovulation undergo development within the oviduct, afloat in a semifluid nutrient mass laden with red blood cells. The embryo of the sting ray feeds on the blood and the secretion provided for it by the slender vascularized glandular structures that grow out from the endometrium and into the uterine cavity. By way of the gill slits, these secretory villi are swallowed into the embryonic gut. Maternal red blood cells are liberated directly into the body of the embryo as well as into its uterine environment. The embryos of the remarkable bony fish Zoarces develop within the ovarian follicles from which the eggs were derived. Here they remain until birth, feeding on the trophic substances provided by the ovarian chamber, rich in maternal blood cells.

Among the placental mammals nutritive materials are supplied to the fetus in two ways: by transmission from the maternal blood circulating through the placenta and by secretions and breakdown products of the endometrium itself. It was first pointed out by Grosser [2] in 1927 that a close relationship exists between the predominant method of nurture of the fetus, on the one hand, and the degree of intimacy between the fetal and maternal bloodstreams, on the other. In the pig, for example, which has an epitheliochorial type of placenta, fetal nutrition is provided for in large measure by the uterine fluids that bathe the chorion. To a lesser degree the uterine milk, or histotrophe, serves as fetal nutriment in the cow, sheep, horse, and goat, which have placentas of the syndesmochorial type. In all of these forms extravasated maternal blood cells have been found, in varying amounts, in the uterine fluids in direct contact with the trophoblast, where they presumably serve as a source of iron and other food essentials for the fetus.[3] In the ass, small effusions of maternal blood have been observed between the endometrium and the chorion, and in some carnivores blood extravasations of greater extent occur regularly along the margins of the placenta. The "green border" of the dog's placenta and the "brown border" of the cat's placenta are examples of these physiological marginal hematomas.

In the primates, which have hemochorial placentas, there is a closer approximation of the fetal and maternal circulations and the uterine fluids play a correspondingly less conspicuous role in fetal nutrition. Even in the primates, however, extravasation of maternal blood into the uterine glands can be observed during the very early stages of gestation. In the rhesus monkey, Wislocki and Streeter recorded the presence of fresh blood deep in some of the endometrial glands near the placental site, traceable to the outlets of the glands and thence to the uterine lumen, the process beginning on the 17th day of pregnancy and continuing for as long as 4 weeks. In most of the well-studied human ova of comparable ages the same phenomenon of bleeding into the glands of the

From the departments of obstetrics and gynecology of the Mount Sinai and Presbyterian hospitals and the College of Physicians and Surgeons, Columbia University.

1. Hartman, C. G.: The Phylogeny of Menstruation, J. A. M. A. 97: 1863-1865 (Dec. 19) 1931.

2. Grosser, O.: Frühentwicklung, Eihautbildung und Placentation des Menschen und der Säugetiere, Munich, J. F. Bergmann, 1927.

3. Amoroso, E. C.: Placentation, in Marshall, F. H. A.: Physiology of Reproduction, Parkes, A. S., editor, ed. 3, London, Longmans, Green & Co., Inc., 1952, vol. 2, pp. 127-311.

endometrium has been observed. Among these ova are the Linzenmeier, Yale, Peters, Edwards-Jones-Brewer, Bryce-Teacher 1, von Möllendorff, and Falkiner specimens.[4]

It might have been predicted from the observations outlined above that some of the maternal blood that is extravasated into the uterine glands in early pregnancy would pass into the lower regions of the genital tract and hence be detectable in the vagina. The first demonstration of red blood cells in the vagina during normal pregnancy was in several strains of rats by Lataste[5] in 1886. This phenomenon was rediscovered in the rat by Long and Evans[6] in 1920. In this species vaginal smears so consistently contain free red corpuscles between the 13th and 16th days of pregnancy that Long and Evans regarded their presence as an infallible sign of pregnancy. The morphological basis for this vaginal bleeding was later described by Stafford[7] and by Venable.[8] By means of intravascular injections of India ink they succeeded in demonstrating the extravasation of maternal blood from the paraplacental border. Localized decidual vessels were seen emptying their contents into the space between the decidua and ectoplacental chorion, whence the blood found its way into the uterine lumen.

By the same technique Stafford showed that the India ink particles were transmitted to special regions of the uterine lumen in the dog and cat, associated with the green and brown borders of the respective placentas of these species. He also found free ink, of paraplacental origin, in the uterine lumen of a rabbit at the 11th day of pregnancy, but failed to demonstrate uterine extravasation of ink in a small series of guinea pigs.

Asdell and Madsen,[9] in a very brief statement in 1933, reported their failure to find microscopic evidence of leakage of red blood cells from the uterus of the pregnant cow. No details were given. Ajello,[10] who later restudied the problem in the cow, reported the vaginal smears to be positive for red blood cells in 5 of 35 cases in which examination was done during the first three months, but negative for red blood cells in 70 cases after the third month of pregnancy.

Carl Hartman's classic studies on the reproductive physiology of the macaque led to the first demonstration of the "placental sign" in a primate. The details of this phenomenon were reported by Hartman in a series of papers dating from 1929 and summarized in his superb monograph of 1932.[11] In a series of 33 accurately dated pregnancies in the rhesus monkey, all but one of the animals presented microscopic evidence of blood in the vaginal washings, beginning at about the time of the first missed menstrual period and continuing for an average of 23 days (range 13 to 32 days). In several cases the bleeding was of sufficient intensity to be detectable macroscopically, and in a few it was indistinguishable in character from a normal menstrual flow.

In a collaborative histological study of serial sections of a macaque uterus at the 29th day of pregnancy, Wislocki and Hartman[12] demonstrated the morphological basis for the observed vaginal bleeding. In one section an intervillous space was seen in direct connection with a uterine gland. Blood could be traced from the oblique glands underlying the placental disks, coursing toward the placental border, through the glandular orifices, and into the uterine lumen.

The possible occurrence of a similar type of uterine bleeding during early pregnancy in the human has been conjectured by Hartman and by Bartelmez.[13] The intrauterine relations in early pregnancy differ, however, in the rhesus monkey and man. In the human, the early sealing off of many of the endometrial glands by the decidua vera and by the fusion of the chorion laeve with the decidua prevents a complete homology between the two species.

BLEEDING IN MAN

The occurrence of bleeding in early pregnancy in women has not received thorough study. In a very brief report in 1931 Kulitzy[14] stated that vaginal smears from 25 women in early pregnancy contained red blood cells in 18 cases. Kulitzy concluded that the vaginal smear was of no value for early diagnosis of pregnancy; otherwise his report is of little value because of its paucity of detail. Ajello refers to some observations of Pensa, who supposedly found red blood cells in 12 of 200 vaginal smears at various stages of pregnancy; but in the absence of a bibliographic reference, efforts to check Pensa's report have been unrewarding.

In the present study, vaginal smears were made in a series of 68 obstetric patients who registered for antenatal care within 60 days of the last normal period. None of the patients had had any macroscopic vaginal bleeding since the onset of pregnancy, and in none were there any visible ulcerative lesions of the cervix or vagina. The group consisted of private and clinic patients who ranged from 19 to 42 years in age and from 0 to 4 in parity.

Smears were made at the first antenatal visit, before manual vaginal examination. An unlubricated speculum was carefully introduced into the vagina, avoiding contact with the cervix. The vaginal mucosa of the posterior fornix was gently swabbed with a cotton-tipped applicator that had been moistened previously with isotonic sodium chloride solution. The smear, made on a glass slide, was allowed to dry in air, stained with Gram stain, and examined microscopically for red blood cells.

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13. Bartelmez, G. W.: Menstruation, Physiol. Rev. **17**: 28-72, 1937.

14. Kulitzy: Das sogenannte Erythrocytenzeichen bei der Frühdiagnose der Schwangerschaft, Zentralbl. f. Gynäk. **55**: 2430-2432, 1931.

Erythrocytes, in varying amounts but usually scant in number, were found in 12, or 18%, of the 68 smears. These positive smears were obtained from patients examined 33, 37, 41, 43, 46, 48, 52 (2 cases), 53, 55, and 57 (2 cases) days after the first day of the last menstrual period. The presence or absence of red blood cells could not be correlated with the age or parity of the patient. Only one of the 12 patients with a positive smear aborted.

The occurrence of macroscopic vaginal bleeding between conception and the 196th day of pregnancy was investigated in another series of 225 consecutive private patients who did not abort. Each patient was seen not later than her second missed menstrual period. She was questioned about any vaginal staining or bleeding previous to this initial interview, including possible causative factors, exact time of occurrence, and the character, color, and amount of the bleeding. She was instructed to report any subsequent staining or bleeding, no matter how slight. This series therefore includes all bleeding detected by the patient, regardless of amount.

Bleeding was reported at some time between the 24th and 196th days of pregnancy by 49, or 21.8%, of the 225 patients. These were divided into five subgroups, as shown in the table.

Type of Nonabortal Macroscopic Bleeding Observed in Early Pregnancy

	No. of Cases	%
Single episode, noncoital, days 24-40	18	8.0
Single episode, noncoital, days 41-196	12	5.4
Coital bleeding (within 8 hours)	5	2.2
Repeated brown noncoital stain	4	1.8
Repeated bright noncoital bleeding	10	4.4
Total no. of cases with bleeding	49	21.8
No. of cases without bleeding	176	78.2

The observation of bleeding was three times as frequent among the multigravidas in this series as among the primigravidas. Of the 132 primigravid patients (58.7% of the total), only 17, or 12.8%, reported bleeding. By contrast, bleeding was observed by 32, or 38.5%, of the 83 multigravidas. This difference is statistically significant, but its biological meaning is not clear.

The cervix of each patient was carefully inspected. Visible lesions were present in only two patients, both of whom noted repeated bright bleeding not associated with coitus. One had a large mucous polyp and the other decidual plaques around the external os.

Thus the bleeding in some of the 49 cases was obviously of pathological rather than physiological origin. Certainly the two patients with the cervical lesions are in the former category, as are also probably the five who bled only after coitus. There remain then 42 patients (18.7%) whose staining or bleeding may have been physiological. By analogy with the monkey it is likely that the single episode of bleeding that began in 18 cases (8%) on or before the 40th day of pregnancy represents a physiological response to implantation. The nature of the bleeding in the remaining 10.7% of the cases is conjectural. Among the 176 cases without bleeding, two cases terminated with abruption of the placenta and one with placenta previa. There were no such complications among the 49 patients who bled.

Current teaching, as revealed by obstetric textbooks, has accorded no place to physiological uterine bleeding in the first trimester of pregnancy. In the clinical literature on obstetric hemorrhage, occasional mention is made of implantation bleeding, believed to be a rare occurrence that results from the invasion and phagocytosis of the endometrium by the trophoblast.[15] Phylogenetic considerations have suggested the probable occurrence in the human of slight bleeding from the endometrium in early pregnancy, and the observations of the present study would tend to confirm this.

The true frequency of this phenomenon in man cannot yet be stated. An accurate estimate would entail repeated observations on the same women, perhaps even daily, beginning at or even before the first missed menstrual period. The single smears on our patients, performed at random dates, thus provide only a minimum figure, probably a gross underestimate of the frequency of physiological bleeding in early pregnancy. Moreover the present series is too small for quantitative significance.

MECHANISM OF BLEEDING

The mechanisms involved in the extravasation of blood from the uterus during the implantation stages of mammals are well established, and the anatomic pathways have already been described. This bleeding is not directly attributable to the erosive action of the trophoblast, however, and can occur in fact independently of the latter. In the rat, for example, the phenomenon is a purely maternal one, since it occurs in pseudopregnant animals with spontaneously developing or experimentally produced deciduomas.[18]

The bleeding associated with implantation differs quantitatively from the bleeding of menstruation in that less blood is shed in association with the former. Bartelmez has ascribed this difference to the corpus luteum of pregnancy, which modifies the vascular reaction of the endometrium and prevents its bleeding, except in the immediate region of the trophoblast, where the latter overcomes the protective action of the corpus luteum.

In the macaque the average interval between the onset of the last menstrual period and the placental sign is 29 days, with a variation comparable to that of the ordinary cycle. Students of menstruation have suggested a fundamental relationship between the two phenomena. Menstruation assumes an adaptive significance when it is visualized as a mechanism for supplying the ovum with free maternal blood. This concept permits an appreciation of the premenstrual endometrial ischemia, a phenomenon well designed to weaken the mucosa in anticipation of the invading trophoblast.

The comparative studies on lower forms, already mentioned, seem clearly to illustrate the functional importance of the extravasation of maternal blood in providing the ovum with nutrient materials. Histological studies on early human ova show much of the blood in the endometrial glands in the process of hemolysis, thereby presenting the components of the erythrocytes to the chorion in soluble form. Early studies on the human placenta by

15. McCormick, C. O., Sr.: Hemorrhage in the First and Second Trimesters, Am. J. Obst. & Gynec. 64A: 349-355, 1952.

Hofbauer [16] have actually demonstrated the uptake of iron by the chorionic villi from the disintegrating maternal erythrocytes in the intervillous spaces.

The physiological bleeding of early pregnancy is of clinical interest from two points of view. Occurring as it often does at about the time of the first missed menstrual period, bleeding that assumes proportions sufficient to be detectable by the patient may result in miscalculation of the duration of pregnancy. Mere spotting or an abbreviated menses is the commoner occurrence at this time, but in some instances the flow may simulate rather perfectly a normal menstrual period. This is the most likely explanation of the enigma commonly encountered by embryologists in cases in which the embryo has attained a stage of development about a month greater than its recorded menstrual age. All obstetricians likewise have had cases in which a term-sized fetus was delivered by the patient a month before her expected date of confinement.

DIFFERENTIATION OF PHYSIOLOGICAL AND PATHOLOGICAL BLEEDING

The differential diagnosis of the physiological from the pathological bleeding of early pregnancy, especially that associated with threatened abortion, is of particular interest to the clinician. In a series of over 700 consecutive private patients studied by us, approximately 28% recognized gross vaginal staining or bleeding at some time between the 25th and 196th days of pregnancy. Abortion occurred in only about one-third of those who stained or bled, while about two-thirds carried to viability.

Several minor clinical considerations aid in the differentiation between the bleeding or staining presaging abortion and that associated with the physiological mechanism of implantation or with some transient pathological process. Nonabortal bleeding is usually slight in amount and is usually not associated with uterine cramps. The truly physiological variety is so scant that it is frequently missed by both the patient and her physician. The bleeding associated with abortion, on the other hand, although it may begin scantily, usually becomes heavier, often with the passage of clots. The character of the bleeding may be helpful in distinguishing between the two conditions. Implantation blood and other nonabortal blood is usually fresh red in color, whereas the early blood of abortion is oftener tan to dark brown.

The presence or absence of nausea and vomiting may also have prognostic value in cases of bleeding in early pregnancy. The outcome of pregnancy was studied in relation to nausea and vomiting in a group of 285 private patients, 60 of whom aborted. Of the 31 patients who aborted within the first trimester of pregnancy, 74% had had no nausea or vomiting whatever. By contrast, of the 225 patients who did not abort, 49 of whom reported some bleeding, only 30% were free of nausea.

These criteria must be evaluated, of course, in relation to the other possible evidences of demise of the conceptus, such as regression of mammary gland changes, failure of the uterus to enlarge, and a new-found feeling of well-being.

No treatment is necessary, of course, for implantation bleeding, which is self-limited and harmless, and there is no specific therapy of proved merit for threatened abortion. From a practical standpoint, therefore, the patient who reports a small amount of fresh-appearing vaginal bleeding early in pregnancy, without uterine cramps, can properly be reassured as to its probable innocent nature, especially if she continues to be nauseated. Only a minority of such patients are destined to abort. On the other hand, the patient who has had no nausea and who begins to bleed with a brown stain has a poor prospect of fetal salvage.

SUMMARY

Comparative embryologic studies have shown extravasation of maternal blood into the brood chamber during pregnancy to be of widespread occurrence among the vertebrates. This bleeding supplements the pabulum with hemic elements and provides an important source of iron for the fetus. In some forms, notably the rat and the macaque, the physiological extravasation of blood into the uterus becomes manifest by the presence of erythrocytes in the vagina and is known as the placental sign.

In the present study, single vaginal smears, taken at random from 68 women between the 33rd and the 60th days of pregnancy (menstrual dates), contained red blood cells in 12 cases, or 18%. Since this is a minimum figure, it is suggested that microscopic bleeding from the uterus actually occurs with greater frequency and that it occasionally assumes macroscopic proportions, even simulating a menstrual flow. This is the most likely explanation of the disparity that sometimes appears between the calculated duration of pregnancy and a disproportionately large fetus.

In another series of 225 consecutive patients who did not abort, macroscopic vaginal bleeding was reported by the patient between conception and the 196th day of pregnancy in 21.8% of the cases. In 8%, the bleeding began on or before the 40th day of pregnancy in the absence of any visible lesion of the cervix and was interpreted as a physiological response to implantation. The physiological bleeding of early pregnancy is distinguished from the bleeding of abortion by the usual association of abortion with a greater flow of blood, the brown-black color of the initial vaginal discharge of blood, uterine cramps, and the absence of nausea.

Fifth Ave. and 100th St. (Dr. Guttmacher).

16. Hofbauer, J.: Grundzüge einer Biologie der menschlichen Plazenta mit besonderer Berücksichtigung der Fragen der fötalen Ernährung, Vienna, Wilhelm Braumüller, 1905, pp. 41-56.

Laboratory Tests.—Nothing is so apt to ruin the practitioner's ability to observe, cripple his logic or lessen clinical experience and sense as routine laboratory work. . . . Laboratory methods should aid in the physician's education and not replace it. . . . A leukocyte count may be high or low or normal in real appendicitis. A four plus Wassermann may be false or a cancer of the lip may be present in a syphilitic with a positive complement-fixation test. . . . Hospitals approved for interne training feel that they are educating physicians for practice, yet they are guilty of a great disservice to these young men by allowing them to order large volumes of laboratory work with very little emphasis on "stop, look and listen" at the bedside, which is so much more important in the interne's training and future success.—E. Kellert, M.D., Laboratory Tests vs. Stethoscopes, *American Practitioner & Digest of Treatment*, July, 1953.

TRENDS IN MATERNAL AND PERINATAL MORTALITY IN NEW YORK CITY

Helen M. Wallace, M.D., Edwin M. Gold, M.D., Leona Baumgartner, M.D., Margaret A. Losty, R.N.
and
Herbert Rich, New York

The New York City program for maternity patients and newborn infants, which operated for a period of over eight years (1944-1951), had the following components, all designed to strengthen the care given to the pregnant woman and her newborn infant: (1) a consultation program designed to improve the quality of antepartum, intrapartum, and postpartum hospital care of the mother and baby[1]; (2) a program designed to improve the level of care of the prematurely born infants [2]; (3) the operation of four antepartum clinics by the New York City Health Department in the low socioeconomic areas of the city and where there was a shortage of hospital facilities; and (4) the supervision of the activities of the midwives remaining in the city and their patients.[3]

With such intensive work over an eight year period, one might reasonably expect that the following objectives were attained, as judged by available data and indexes: (1) a lowering of the maternal mortality rate; (2) a lowering of the neonatal mortality rate; (3) for fetal deaths, a decreasing ratio to live births, a prolongation of those pregnancies terminating in early fetal death with fewer fetal deaths occurring early in pregnancy, and a change in the weight distribution, with fewer fetal deaths occurring in the lower weight groups; and (4) for premature infants, a lower incidence of premature births, lower mortality rate in premature infants, and a change in the birth-weight distribution with fewer premature infants born in the lower weight groups. These factual indexes may demonstrate the degree of effectiveness of this eight year program.

MATERNAL AND NEONATAL MORTALITY

During the period 1945-1951, the maternal mortality rate decreased 62.5%, the postneonatal (1 through 12 months of age) mortality rate 37.3%, and the neonatal mortality rate 16.7%. Detailed studies of maternal deaths in 1947,[4] 1948, and 1949 [5] revealed that the deaths due to hemorrhage, infection, and cardiovascular disease showed the major decrease. In this three year period, deaths due to toxemia increased, while deaths due to anesthesia remained at a plateau (table 1). The decrease in maternal mortality due to hemorrhage was directly related to the increased provision and immediate availability of blood within the hospitals; this need was emphasized greatly at the time surveys of the hospitals were made by the health department consulting staff. The decrease in maternal mortality due to infection was undoubtedly related to the use of antibacterial agents. The fact that toxemia as a cause of maternal mortality remained reasonably static may have been related to the increased birth rate during this period with the resultant increased load of patients on already burdened hospital antepartum clinics. It also may have been related to the recent influx of Puerto Ricans. The fact that anesthesia as a cause of maternal mortality remained stationary was undoubtedly related to the small percentage of maternity services staffed by qualified anesthetists.

TABLE 1.—*Maternal Deaths per 10,000 Live Births in New York City, by Cause**

Cause	1947		1948		1949	
	No.	Rate	No.	Rate	No.	Rate
Hemorrhage	53	3.1	46	3.0	35	2.2
Infection	48	2.8	44	2.8	33	2.1
Cardiovascular disease	42	2.4	23	1.5	33	2.1
Toxemia	27	1.6	22	1.4	31	2.0
Anesthesia	10	0.6	12	0.8	8	0.5
Miscellaneous	47	2.7	52	3.3	51	3.2
Unknown	3	†	12	0.8	12	0.8
Total	230	13.2	211	13.6	201	12.9

* Gold and Wallace.[4] Faison.[5]
† Fewer than 0.05 per 10,000 live births.

An analysis of the causes of neonatal mortality from 1945 to 1951 reveals that deaths attributed to birth injury, congenital malformations, gastrointestinal diseases (primarily diarrhea), other diseases peculiar to the first year of life, and all other deaths decreased. Deaths due to bronchopneumonia and other respiratory diseases increased, while deaths due to prematurity remained stationary (table 2). The decrease in neonatal mortality attributed to birth injury may have been a result of the intensive effort of the hospital staffs and the city health department with the assistance of its advisory obstetric committee to strengthen the quality of obstetric care in the city through the establishment of indications for the use of consultation with a qualified obstetrician in the management of certain obstetric patients. The decrease in neonatal mortality due to gastrointestinal diseases was the result of increased effort on the part of hospital staffs to reduce overcrowding in nurseries, provision of the care of the infant on an individualized basis, and improved nursing procedures within the nurseries. Earlier

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6. Deleted on proof.

and better reporting of infections among newborn infants to the city health department by hospitals and steps taken by the hospital staffs to segregate infected or "suspect" infants undoubtedly contributed to this reduction.

FETAL DEATHS

Since 1938 all products of conception, regardless of the length of gestation, have been reportable in New York City. Table 3 indicates that there has been a 31% increase in the reported fetal death ratio in 1950 as compared with 1945. Whether this increase is a true one or is a result of better reporting of fetal deaths is unknown. A previous study [7] with data from the Emergency Maternity and Infant Care (EMIC) Program indicated that the incompleteness of reporting of fetal deaths in New York City was about 50%. After publication of the study, some work was done with the hospitals and with the medical profession to secure better reporting. It is, therefore, possible that the increase in the fetal death rates might be related to the factor of reporting.

If our premise is correct, one of the anticipated effects of an intensive program for maternity patients and newborn infants would be the prolongation of fetal life—in other words, fewer fetal deaths occurring early in pregnancy. Table 3 shows that the anticipated trend did not occur. In fact, the reverse happened; an increasing percentage of fetal deaths early in pregnancy (under 20 weeks) was reported. Whether this finding was related to better reporting of early fetal deaths is unknown.

Furthermore, if the premise is correct, another expected result would be the decrease in the percentage of fetal deaths reported in the groups with lower weight. There was a decrease in the percentage of fetal deaths in all groups with weight reported and an increase in the fetal deaths in groups with weights not reported. The group with weight not stated (84% of the total fetal deaths in 1950) illustrates inadequate reporting.

TABLE 2.—*Neonatal Deaths and Neonatal Mortality Rates per 1,000 Live Births in New York City, by Cause*

Cause	1945		1946		1947		1948		1949		1950		1951	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
Prematurity	1,421	11.0	1,735	11.4	1,682	9.9	1,680	10.6	1,540	9.8	1,603	10.3	1,628	10.0
Birth injury	427	3.3	446	2.9	542	3.2	456	2.9	427	2.7	398	2.6	409	2.5
Congenital malformations	412	3.2	450	2.9	537	3.1	461	2.9	425	2.7	398	2.6	409	2.5
Other diseases peculiar to first year of life	356	2.8	399	2.6	381	2.2	330	2.1	357	2.3	326	2.1	328	2.0
Bronchopneumonia and other respiratory disease	100	0.8	136	0.9	186	1.1	155	1.0	133	0.8	174	1.1	166	1.0
Gastrointestinal diseases	72	0.5	58	0.4	55	0.3	23	0.2	40	0.3	12	0.1	16	0.1
All other causes	62	0.5	60	0.4	59	0.4	69	0.4	76	0.5	60	0.3	42	0.3
Total	2,850	22.1	3,279	21.5	3,442	20.1	3,174	20.1	2,998	19.1	2,971	19.1	2,998	18.4

TABLE 3.—*Reported Fetal Deaths in New York City, by Length of Gestation*

Length of Gestation	1945		1946		1947		1948		1949		1950	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Under 20	6,448	62.2	8,369	64.5	9,188	65.3	9,454	67.4	10,234	70.8	12,255	74.7
20-27	1,151	11.1	1,471	11.3	1,529	10.9	1,499	10.7	1,369	9.5	1,337	8.1
28-39	1,371	13.2	1,592	12.3	1,627	11.5	1,463	10.4	1,399	9.7	1,289	7.9
40-43	1,198	11.6	1,313	10.1	1,377	9.8	1,206	8.6	1,150	7.9	1,009	6.1
44 and over	32	0.3	42	0.3	52	0.4	35	0.3	30	0.2	30	0.2
Not stated	167	1.6	193	1.5	304	2.1	361	2.6	273	1.9	485	3.0
Total	10,367	100	12,980	100	14,077	100	14,018	100	14,455	100	16,405	100
Ratio to 1,000 live births	80.5		85.0		82.2		88.7		92.1		105.3	

TABLE 4.—*Premature Infants Born Alive in New York City, by Birth Weight*

Birth Weight, Gm.	1945		1946		1947		1948		1949		1950		1951	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Under 1,000	457	4.4	593	4.7	584	4.2	563	4.4	611	4.8	745	5.6	842	5.9
1,000-1,499	700	6.8	827	6.5	859	6.2	816	6.4	792	6.1	855	6.5	954	6.7
1,500-1,999	1,824	17.8	2,173	17.2	2,307	16.8	2,231	17.4	2,255	17.5	2,329	17.6	2,418	17.0
2,000-2,499	7,263	71.0	9,051	71.6	10,032	72.8	9,203	71.8	9,226	71.6	9,270	70.3	9,983	70.4
Totals	10,244	100	12,644	100	13,782	100	12,813	100	12,884	100	13,199	100	14,197	100

TABLE 5.—*Deaths in New York City of Premature Infants in First Year of Life, by Birth Weight*

Birth Weight, Gm.	1945		1946		1947		1948		1949		1950		1951	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Under 1,000	439	96	549	92.6	546	93.5	521	92.5	500	91.7	678	91.0	767	91.1
1,000-1,499	433	62	470	56.8	471	54.8	432	52.9	354	44.7	368	43.0	473	49.6
1,500-1,999	417	23	425	19.6	416	18.0	433	19.4	370	16.4	365	15.7	382	15.8
2,000-2,499	459	6	467	5.1	491	4.9	438	4.8	415	4.5	407	4.4	409	4.1
Totals	1,748	17	1,911	15.1	1,924	14.0	1,824	14.2	1,699	13.2	1,618	13.8	2,031	14.3

7. Baumgartner, L.; Wallace, H. M.; Landsberg, E., and Pessin, V.: The Inadequacy of Routine Reporting of Fetal Deaths, Am. J. Pub Health **39**: 1549-1552 (Dec.) 1949.

PREMATURE INFANTS

The supplementary portion of the live-birth certificate in New York City has had an item regarding birth weight since 1938. The birth weight of over 99% of all live-born infants in New York City is now recorded on the birth certificates. In the period 1940-1951, the incidence of premature birth increased significantly. In the period 1945-1951, the birth-weight distribution of premature infants remained unchanged except for an increase in live births in the group with weight under 1,000 gm. (about 2 lb.). (table 4.).

The mortality percentage among premature infants, however, declined in this same period of time. This decline occurred in all groups of premature infants, but the decline was least in the group with weight under 1,000 gm. This decline reflected the increased interest among physicians, nurses, and hospital administrators in the problem of the care of premature infants and the provision of a better quality of care for such infants. During this period, standards for the care of premature infants were developed by the health department with the assistance of its pediatric advisory committee, and the city-wide program for prematurely born infants was begun with the establishment of special centers (table 5).

It is usually agreed that, weight for weight, the nonwhite premature infant is more mature and has a better chance of survival than the white infant. In the New York City data, this fact was true only in the group of premature infants with the lowest weight (under 1,000 gm.). In all other weight groups, the white premature infant mortality rate was better than the nonwhite through 1948. Since that time, a pattern has developed in which the nonwhite premature infants have shown a better survival rate than the white. These facts reflect current findings in hospitals in the city. In 1950, two municipal hospitals, caring for nonwhite patients almost exclusively, developed centers for premature infants; in 1952, an additional municipal hospital, predominantly caring for nonwhite patients, also developed a center for premature infants.

COMMENT

The foregoing facts may be summarized as follows: 1. There has been a significant decline in maternal and postneonatal mortality in New York City; the decline in neonatal mortality, although it has occurred, has been less. 2. There has been no similar change in the fetal death rate or in the duration of pregnancies terminating in fetal death, as demonstrated by the time of occurrence of the fetal deaths or the weights. 3. There has been no decline in the incidence of premature birth or no change in the birth-weight distribution of premature infants born alive except for an increase in live births in the group with weight under 1,000 gm. 4. The infant mortality among premature infants has declined in all birth-weight groups, reflecting the intensive work done by physicians, nurses, and hospitals in the city-wide program for premature infants. 5. Contrary to most reports, the nonwhite premature infant has been in a disadvantageous position compared with the white, as reflected in mortality through 1948; since that time the nonwhite premature infants have shown a better survival rate than the white.

These facts reflect current findings in hospital care in New York City.[8] The general impression gleaned from hospital surveys and conferences with hospital personnel over this eight year period is that, while there has been considerable improvement in the inpatient hospital care of the maternity patient and her newborn infant, there has been little or no improvement in hospital antepartum clinics. The same problems remain regarding overcrowding of clinics; understaffing by physicians and nurses; long lines of patients waiting to be seen by the physicians; inadequate antepartum care according to accepted standards; little or no counseling of the patient; little or no attention paid to maternal nutrition, and little or no privacy afforded the patient or other satisfying experiences that would tend to induce the pregnant woman to register early for her antepartum care and to continue it without interruption during her pregnancy. Certainly, it is not unreasonable to expect that, if adequate antepartum care were provided for all pregnant women in the community, the fetal death rate and the incidence of premature birth might be favorably affected. The fact that a special program can accomplish its desired objectives of providing better care and saving more lives has been amply demonstrated even in this short time in the New York City program for prematurely born infants.

It is evident that in the broad consideration of the care of mothers and newly born infants, the outcome of all pregnancies should be studied. This means that the deaths of fetuses in utero, prior to or during delivery, as well as the survival of the parturient woman and her live-born infant, must be studied. There is considerable evidence that many of the factors contributing to early neonatal deaths may be the same ones contributing to fetal deaths, either directly or indirectly. An artificial pattern, primarily for statistical purposes, has been used for many years, namely, that of considering separately the problem of fetal deaths and that of early neonatal deaths. This custom has been a completely artificial one, and it seems clear that the problem of total pregnancy wastage must be considered together. Gradually the term "perinatal" mortality is coming into usage to embrace this larger concept. One other finding in this study is the need to encourage better reporting of the weights of products of conception or dead fetuses, since almost four-fifths of the fetal death certificates contain no data on weight. Above all there is the need of greater interest and research into the entire problem of the causes and prevention of fetal death and premature birth. The two leads of better care and more research should probably be followed simultaneously if the objective of saving additional lives as quickly as possible is to be achieved.

SUMMARY

In recent years, there has been an intensive program in New York City to improve the care of maternity patients and their newborn infants. Some gains have been made, particularly in the following areas: (1) reduction of maternal mortality due to hemorrhage and infection; (2) reduction in postneonatal mortality; (3) reduction in neonatal mortality attributed to birth injury, congen-

8. New York Academy of Medicine, Committee on Public Health Relations: Infant and Maternal Care in New York City, New York, Columbia University Press, 1952.

ital malformations, and gastrointestinal disease; (4) reduction in the infant mortality rate in premature infants born alive. On the other hand, the following areas have shown no progress: (1) reduction in the ratio of fetal deaths to live births; (2) prolongation of pregnancies terminating in fewer early fetal deaths and fewer fetal deaths occurring in the groups with lower weight; (3) reduction in the incidence of premature births; (4) change in the birth-weight distribution of prematurely born infants, with fewer infants born in the groups with lower weight.

125 Worth St. (Dr. Wallace).

ASSOCIATION OF MATERNAL AND FETAL FACTORS WITH THE DEVELOPMENT OF EPILEPSY

1. ABNORMALITIES IN THE PRENATAL AND PARANATAL PERIODS

Abraham M. Lilienfeld, M.D.
and
Benjamin Pasamanick, M.D., Baltimore

There exist two schools of thought concerning the relative importance of heredity and brain damage as causal factors in the development of epileptic seizures. The proponents of a genetic hypothesis maintain that in a majority of cases epilepsy or the tendency to have epilepsy is inherited as a recessive trait. On the other hand, proponents of the brain injury hypothesis state that in most cases anoxia during the prenatal and paranatal periods has resulted in brain damage, which in turn is the basic cause of the convulsive seizures. The evidence on which these differing hypotheses are based might be divided into three types: clinical, experimental, and pathological.

The clinical evidence consists of the determination of frequency of a family history of epilepsy and frequency of brain injury among a group of epileptic patients. For example, Lennox found that, in a group of 2,053 patients, 37% had a family history of epilepsy, 14% had a history of preceding pathological conditions in the brain, 10% had a history of both, and in 39% no cause could be ascertained. Thus in this large series of patients, 76% had no evidence of pathological conditions of the brain while 24% had such evidence.[1] On the other hand Bridge, in studying a series of 742 patients, found that in 14% there was what he termed a hereditary factor, in 41% there was a brain injury factor, in 29% both factors were operative, and in 16% neither of the factors was found.[2] In this series 30% had no history of brain injury, while 70% had such a history. There are obvious uncertainties in making inferences from these data. It is rather difficult to determine from the published report what Lennox meant by brain injury. Bridge, however, gave the various subcategories that he collectively categorized as brain injury, but these suffer from the limitation that they were obtained by questioning the mother concerning events during the prenatal and paranatal periods that probably had occurred several years prior to the time of interview. In addition, there is no control group with which the frequencies can be compared. To support the validity of his hypothesis, Lennox utilizes data obtained from studies on twins and familial aggregation. We will consider these later in this report. Fender, realizing some of these limitations, obtained a history of events occurring during pregnancy and delivery in a group of 37 epileptic patients; 25 had histories of complications of pregnancy and labor.[3] In a control group of 40 children with rheumatic fever, appendicitis, and fractures, only 4 had abnormal birth histories. The results are suggestive, but the small size of the series, the questionable adequacy of the control group, and the source of the histories limit the inferences that can be drawn from these data.

Fender expanded his approach to include an experimental one. He subjected pregnant bitches to 4% oxygen levels. Out of 23 pups 18 died, 3 were normal, and 2 had convulsions. Windle has obtained similar results from experiments on guinea pigs.[4] Only limited inferences can be made from such experiments, particularly with regard to applying them to human experience.

Pathological evidence has been accumulating during the past few years that seems to indicate that the types of lesions found in selected epileptic patients are probably the result of brain damage incurred during birth or infancy.[5] Recently Earle, Baldwin, and Penfield reported that 63% of cases of temporal lobe seizures were probably caused by compression or anoxia of the brain during birth or in infancy.[6] Most of these pathological studies depend on identifying a histological lesion that is considered to be characteristic of anoxia. Substantiation that this method is valid was obtained from examination of lesions that were experimentally produced. Although

From the departments of epidemiology and public health administration (Division of Mental Hygiene), Johns Hopkins School of Hygiene and Public Health.

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1. Lennox, W. G.: The Heredity of Epilepsy as Told by Relatives and Twins, J. A. M. A. **146**: 529-536 (June 9) 1951.

2. Bridge, E. M.: Epilepsy and Convulsive Disorders in Children, New York, McGraw-Hill Book Company, Inc., 1949.

3. Fender, F. A.: Anoxia and the Convulsive State, California Med. **71**: 103-105 (Aug.) 1949.

4. Windle, W. F.: Asphyxia Neonatorum: Its Relation to the Fetal Blood, Circulation and Respiration and its Effect upon the Brain, edited by R. F. Pitts, Springfield, Ill., Charles C Thomas, Publisher, 1950.

5. Nielsen, J. M., and Courville, C. B.: Role of Birth Injury and Asphyxia in Idiopathic Epilepsy, Neurology **1**: 48-52 (Jan.-Feb.) 1951.

6. Earle, K. M.; Baldwin, M., and Penfield, W.: Incisural Sclerosis and Temporal Lobe Seizures Produced by Hippocampal Herniation at Birth, A. M. A. Arch. Neurol. & Psychiat. **69**: 27-42 (Jan.) 1953.

such evidence may be considered as being suggestive, the fact that these patients are a highly selected group and the lack of suitable controls again limit the inferences that can be made from such investigations. Courville has recently reviewed the evidence concerning this aspect of the problem.[7]

It seems that a better approach to the question of the association of maternal and fetal factors with the development of epilepsy might be made by selecting a group of epileptics born in a given area and then reviewing the maternal and fetal factors as recorded on birth certificates and hospital obstetric records. Comparison could then be made with an appropriately selected control group. Such an approach has recently been used in a similar study of the association of maternal and fetal factors with the development of cerebral palsy.[8] This is a report of the results of such an investigation with regard to epilepsy.

METHOD OF STUDY

The case registers of the Epilepsy Clinic and the Harriet Lane Home of the Johns Hopkins Hospital, the Epilepsy Clinic of the University Hospital, and the Neurology Clinic of the Baltimore City Hospitals were searched for the names and identifying information of all patients with diagnosed epilepsy who were born during the period from 1935 to 1952 inclusive. The registers of two institutions for mental defectives operated by the State of Maryland Department of Mental Hygiene were likewise searched for institutionalized persons with epilepsy. The following information concerning each case was obtained from the clinic or hospital record when available: age of onset, type of epilepsy, presence of associated defects such as mental deficiency, cerebral palsy, or other defects, and the results of electroencephalographic examination. The records obtained from these different institutions were matched to locate duplicates, which were discarded. The birth register maintained by the Bureau of Vital Records of the Baltimore City Health Department was then searched for the birth certificates of these persons. As a control series of births with which the epilepsy cases could be compared, the next birth reported from the same place of birth as the epilepsy case, matched by race and maternal age group, was selected. The maternal age groups used were the following: under 20, 20 to 24, 25 to 29, 30 to 34, 35 and over. Initially, an attempt was also made to match the controls by birth order. However, the time spent in locating a certificate with this additional characteristic seemed completely out of proportion to the gain that would result. It was later found that the distribution of the epileptic children and their matched controls according to birth order was similar, as one would expect from the correlation that exists between maternal age and birth order. If the matched control had died during the neonatal period as determined either from the birth certificate or from the hospital record, this birth was omitted from the control series and the next birth with the characteristics noted above was selected. This was done since in a child dying during the neonatal period there was no chance that epilepsy would develop and this child should not, therefore, be considered as a control whose prenatal and paranatal experiences could be compared with an epileptic child who had survived the neonatal period. From the birth certificates the following information was obtained on each epileptic and his matched control: place of birth, maternal age, total number of previous pregnancies, number of previous infants born alive and now living, the number born alive and now dead, and number born dead.

In those instances where the epileptic child and its matched control were born in a hospital, the following information concerning the pregnancy and delivery was abstracted from the hospital record: total number of previous pregnancies of the mother, numbers of previous abortions, previous stillbirths, previous premature births, previous neonatal deaths, length of labor, complications of pregnancy and labor, operative procedures, birth weight, and the condition of child during the neonatal period. The person obtaining this information from the hospital record was not informed whether the birth was of an epileptic or of a control child. The hospital records did not contain information concerning the abnormalities studied on a small number of persons with epilepsy and of the controls. The size of this group varied depending on the specific abnormality, resulting in a slight variation in the totals in the tables presented in this report.

Of the 564 epileptic children for whom birth certificates were located 190, or 33.7%, were nonwhite. Seventy-five per cent and 66%, respectively, of white and nonwhite births were in hospitals. Seventeen children, representing 3.0% of the total, were a result of a multiple pregnancy. It is of interest that this percentage of multiple births is higher than in the control group (1.2%) and in the general population (1.2%). This report will be concerned with the single birth group, since the number of multiple births is so small. Of the 374 white epileptics 218, or 58.3%, were males. On the other hand, of the 190 nonwhite epileptics 95, or 50%, were males. It would appear that in white males epilepsy was more liable to develop. A higher proportion of males among a group of cerebral palsy patients has been previously noted.[8]

One might question the reliability of inferences drawn from epilepsy cases that were principally obtained from a clinic population and that consequently would appear to have an over-representation of persons in the lower income groups. It was possible to examine this point by utilizing census tract information that permitted the grouping of the cases into various economic categories. The epileptic children and their matched controls were essentially similar in this respect.

In this report, consideration will be limited to the association of complications of pregnancy and parturition, prematurity, and abnormal neonatal conditions with the development of epilepsy. The results of the study of the association with other maternal and fetal factors will be presented in subsequent reports. The factors that are analyzed in this report were available only for births in hospitals, thereby reducing the number of white cases from 374 to approximately 274 and nonwhite cases from 190 to approximately 122. A certain number of hospital records did not have complete information for all of the

7. Courville, C. B.: Contributions to the Study of Cerebral Anoxia, Los Angeles, San Lucas Press, 1953.

8. Lilienfeld, A. M., and Parkhurst, E.: A Study of the Association of Factors of Pregnancy and Parturition with the Development of Cerebral Palsy: Preliminary Report, Am. J. Hyg. 53: 262-282 (May) 1951.

factors studied. In the analysis these have been omitted in each instance. Consequently, the total number of cases studied for each factor differ slightly.

COMPLICATIONS OF PREGNANCY AND PARTURITION

A comparison of the distribution of the various complications of pregnancy and parturition that had occurred among mothers of the epileptic children and the matched controls of both races is presented in table 1. In view of the fact that many mothers have more than one complication, a frequency distribution of children according to the number of maternal complications is presented for these groups in table 2. From these comparisons we note that for the white epileptic patients the percentage of mothers with one or more complications is 27.7% as compared to 18.8% for the control children, a difference that is statistically significant. (In this report differences will be considered statistically significant at a probability level of .05.) In the nonwhite group 50.8% of mothers of epileptics had one or more complications as compared to 43.4% of mothers of the controls. This difference is not significant, although it is in the same direction as that found among the whites.

An attempt was made to see whether the nonwhites differed from the whites with regard to a characteristic that might explain this difference. We found that 35% of the white epileptic patients had associated defects such as cerebral palsy and mental deficiency as compared to 16% of the nonwhites. Since these associated defects may be related to the factors being studied, the data were analyzed with the white and nonwhite epileptic children being subdivided into those with and without associated defects. These results are presented in tables 1 and 2. It is apparent that this does not change the differences noted above.

It is interesting that among the epileptic patients there appear to be more who had been exposed to multiple maternal complications than among the controls. Eight per cent of the white persons with epilepsy had been exposed to two or more maternal complications as compared to 2.2% of the controls, and 18.0% of the nonwhite persons with epilepsy had been exposed to two or more complications as compared to 11.5% of the controls. In viewing the specific types of maternal complications presented in table 1 we note that those that appear to be more highly associated with epilepsy are the toxemias and placental abnormalities such as bleeding during pregnancy (cause not specified) and placenta previa. These complications are more prone to produce fetal anoxia and, as reported previously, they are more highly

TABLE 1.—*Specific Complications of Pregnancy Among Mothers of Persons with Epilepsy and Mothers of Their Matched Controls, by Race and Presence of Associated Defects*

Maternal Complication	White				Nonwhite		
	Number of Persons with Epilepsy				Number of Persons with Epilepsy		
	Without Associated Defects *	With Associated Defects	Total	Number of Control Births	Without Associated Defects	Total	Number of Control Births
Toxemias of pregnancy	28	9	37	20	28	28	23
Bleeding during pregnancy and labor (cause not specified)	10	2	12	1	2	3	4
Nonpuerperal complications †	8	4	12	9	28	29	21
Breech presentation	7	2	9	8	0	5	0
Dystocia owing to abnormal pelvis	6	2	8	12	13	13	16
Miscellaneous puerperal complications ‡	1	5	6	1	6	8	0
Premature separation of placenta	3	2	5	2	1	1	1
Dystocia other than owing to abnormal pelvis	2	3	5	2	0	1	0
Placenta praevia	3	1	4	1	0	1	1
Prolapse of cord	1	2	3	1	0	0	1
Malpresentations other than breech	0	1	1	0	0	0	1
Total number of hospital records containing information	183	91	274	271	109	122	122

* Associated defects include cerebral palsy, mental deficiency, and malformations.
† Nonpuerperal complications include diseases associated with, but not related to, pregnancy.
‡ Miscellaneous puerperal complications include pyelitis, other genitourinary diseases, and hydramnios.

TABLE 2.—*Frequency of Complications of Pregnancy Among Mothers of Persons with Epilepsy and Among Mothers of Their Matched Controls, by Race and Presence of Associated Defects*

No. of Maternal Complications	White								Nonwhite					
	No. of Epilepsy Patients								No. of Epilepsy Patients					
	Without Associated Defects		With Associated Defects		Total		Number of Control Births		Without Associated Defects		Total		Number of Control Births	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
0	133	72.7	65	71.4	198	72.3	220	81.2	58	53.2	61	50.0	69	56.6
1	34	18.6	20	22.0	54	19.7	45	16.6	29	26.6	39	32.0	39	32.0
2	13	7.1	5	5.5	18	6.6	6	2.2	17	15.6	17	13.9	13	10.6
3	3	1.6	1	1.1	4	1.4	...	....	5	4.6	4	3.3	1	0.8
4	...	....	..	....	...	....	...	....	..	....	1	0.8	..	....
Total	183	100.0	91	100.0	274	100.0	271	100.0	109	100.0	122	100.0	122	100.0
No. having one or more complications	50	27.3	26	28.6	76	27.7	51	18.9	51	46.8	61	50.0	53	43.4
No. having two or more complications	16	8.7	6	6.6	22	8.0	6	2.2	22	20.2	22	18.0	14	11.5

associated with the development of cerebral palsy and fetal loss than complications that are more prone to produce mechanical trauma.[8]

PREMATURITY

In view of the previously observed relationships of prematurity with cerebral palsy and because of the clinical observations that premature infants are more susceptible to anoxia, a comparison of the prevalence of prematurity among the cases of epilepsy with the controls was made. Since complications are associated with prematurity, it was necessary to make this comparison according to the presence or absence of complications. The results are presented in table 3. The percentage of premature babies (those with birth weights below 2,500 gm.) among the white persons with epilepsy with complications was 25.4%, while it was 8.3% among those without complications. The percentage of premature babies among the controls with complications was 6.4%, and it was 3.2% among those without complications. In both the group with complications and the group with no complications, the prevalence of prematurity was significantly higher in the white persons with epilepsy than in the control group. The prevalence of prematurity was greater among the nonwhites with epilepsy than among the controls, but the differences were not statistically significant.

It appears that prematurity is associated with the development of epilepsy and this association is independent of whether or not prematurity is a result of a complication of pregnancy or parturition.

PRESENCE OF ABNORMAL NEONATAL FINDINGS

From the hospital records information was obtained concerning the status of the infant during the neonatal period. Infant abnormalities that were considered were convulsions, cyanosis, and asphyxia. Corroboration of the clinical impressions was obtained by information concerning the need for oxygen. It is generally accepted that such conditions are under-reported on the hospital record, except for the more severe forms.

The prevalence of these neonatal abnormalities among epileptics and controls for both races is presented in table 4. From this we note that 5.7% of white controls had neonatal abnormalities as compared to 17.2% of white persons with epilepsy, and 3.3% of nonwhite controls had abnormalities as compared to 13.6% of nonwhite epileptics. All of these differences are statistically significant.

In view of the fact that these neonatal abnormalities are associated with both prematurity and maternal complications, we thought it would be desirable to summarize the prenatal and paranatal factors presented by disregarding the overlapping that occurs between these conditions. Thus, we would consider only those children who were exposed to one or more complications, prematurity without maternal complications, and neonatal abnormalities without either maternal complications or prematurity. We would thus obtain an estimate of the total frequency of abnormal prenatal and paranatal factors in each of our groups. Such a compilation is presented in table 5. In our white group, 39.4% of epileptic children

TABLE 3.—*Comparison of Percentage of Premature Births (Birth Weight Below 2,500 Gm.) Among Epilepsy Patients and Control Births According to Presence of Maternal Complications of Pregnancy and Parturition, by Race*

	Maternal Complications Present			Maternal Complications Absent			Total		
		Premature Births			Premature Births			Premature Births	
	Total Births	No.	%	Total Births	No.	%	Total Births	No.	%
White									
Epilepsy patients	71	18	25.4	192	16	8.3	263	34	12.9
Control births	47	3	6.4	217	7	3.2	264	10	3.8
Nonwhite									
Epilepsy patients	56	11	19.6	66	8	11.8	122	19	15.3
Control births	53	9	17.0	68	6	8.8	121	15	12.3

TABLE 5.—*Frequency of Various Abnormalities of Prenatal and Paranatal Periods Among Epilepsy Patients and Control Births, by Race and Presence of Associated Defects*

	White								Nonwhite					
	Epilepsy Patients								Epilepsy Patients					
	Without Associated Defects *		With Associated Defects		Total		Control Births		Without Associated Defects		Total		Control Births	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Total with one or more maternal complications at pregnancy	50	27.3	26	28.6	76	27.7	51	18.8	51	46.8	60	49.2	53	43.5
Total premature births without maternal complications	4	2.2	11	12.1	15	5.5	7	2.6	5	4.6	8	6.6	6	4.9
Total with abnormal conditions during neonatal period without prematurity or maternal complications †	8	4.4	9	9.9	17	6.2	9	3.3	4	3.7	5	4.1	2	1.6
Total with abnormalities of prenatal and paranatal period	62	33.9	46	50.6	108	39.4	67	24.7	60	55.1	73	59.9	61	50.0
Total	183	100.0	91	100.0	274	100.0	271	100.0	109	100.0	122	100.0	122	100.0

* Associated defects include cerebral palsy, mental deficiency, and malformations.
† Abnormal conditions during neonatal period include convulsions, cyanosis, and asphyxia.

have been exposed to one or more of these abnormalities. However, when this group is divided into those with and those without associated defects, we find that 33.9% of those without associated defects have one or more abnormalities as compared to 50.5% of those with associated defects. These are to be compared with a prevalence of these abnormalities of 24.7% among our controls. The prevalence of these abnormalities among all of the nonwhite cases is 59.8% and 55.0% among those without associated defects as compared to 50.0% among controls. The differences between white epileptics and controls are statistically significant. The differences found between the nonwhite epileptics and controls are not significant although they are in the same direction as was found among the whites.

RELATIONSHIP TO EPILEPSY IN PARENTS

We thought it would be of considerable interest to see if the percentage of epileptic parents of the persons with epilepsy varied in groups of persons with epilepsy categorized according to the presence of these prenatal and paranatal factors. Consideration was limited to the prevalence of affected parents rather than the presence of a positive family history in general, since the question of a positive family history is rather vague if one does not determine an actual frequency among a well-defined group of relatives, which was not possible with our data. In addition, family history as such is influenced by factors of memory, social relationship, and other considerations. The prevalence of affected parents in the total group of patients, in those with no associated defects, in those with no complications, and in those without premature delivery, is presented in table 6 for both races. Among the whites the prevalence varies between 4.8% and 5.8%, and among the nonwhites between 4.1% and 4.3%. The constancy of this prevalence ratio is striking. These results are contrary to those obtained by Lennox, who finds a much lower prevalence of birth injury among those with a positive family history than in those with a negative family history.[1] Admittedly these results are not completely comparable, because in this report consideration was limited to the parents.

It was possible to compare the group of persons with epilepsy with the controls with regard to duration of labor and the types of operative procedures performed at time of delivery of these children. No essential differences were noted in either race.

TABLE 4.—*Occurrence of Abnormal Conditions During Neonatal Period of Persons with Epilepsy and Control Births, by Race*

	White				Nonwhite			
	Epilepsy Patients		Control Births		Epilepsy Patients		Control Births	
	No.	%	No.	%	No.	%	No.	%
Normal condition during neonatal period	216	82.8	250	94.3	102	86.4	117	96.7
Abnormal condition during neonatal period *	45	17.2	15	5.7	16	13.6	4	3.3
Total for whom condition during neonatal period was stated	261	100.0	265	100.0	118	100.0	121	100.0

* Abnormal condition includes convulsions, cyanosis, and asphyxia.

COMMENT

The results of this study appear to indicate that there exists a relationship between certain abnormal conditions associated with childbearing and the subsequent development of epilepsy in the offspring. It is well to point out that there are limitations to the inferences that can be drawn from this retrospective study. One difficulty results from the fact that the association was not clearly evident in the nonwhite group. However, it must be granted that in the nonwhite group the differences between epileptic persons and their matched controls are all in the same direction as was observed in the white group. One possible reason for this may be that the size of the nonwhite group is too small to be able to detect a difference. Unfortunately, it was not practical to increase the size of the series to test this point adequately.

Another possible explanation for this may be that postnatal factors may be more frequent in the nonwhite group, and consequently any differences that exist between the control groups and the groups of epileptics might be diluted. In this report we have not discussed postnatal conditions such as lead poisoning or head injury that may be causal factors in epilepsy. How important they are is not certain but there does not seem to be any doubt that they exist.[2] We have not eliminated any of the epilepsy cases in our series when it was thought that a postnatal condition might be the cause of the seizures, since this may have resulted in a bias in favor of the association with those factors studied. It is important to point out, however, that the inclusion of such cases tends to diminish the association with prenatal and paranatal factors, and, therefore, if it were possible to eliminate these cases, the association we have found would have been greater.

The pattern of factors such as complications of pregnancy, prematurity, and neonatal abnormalities that appear to be associated with epilepsy is similar to that previously found to be associated with cerebral palsy, stillbirths, and neonatal deaths. It has been postulated that there exists a continuum of reproductive casualty composed of a lethal component consisting of stillbirths,

TABLE 6.—*Prevalence of Parents with Epilepsy Among Epilepsy Patients According to Association with Other Defects or Abnormalities of Prenatal and Paranatal Period by Race*

	Number of Epilepsy Patients	Number of Parents of Persons with Epilepsy	Parents with Epilepsy	
			No.	%
White				
All patients	324	648	31	4.8
Patients without associated defects *	216	432	25	5.8
Patients without maternal complications	184	368	20	5.4
Patients not born prematurely	209	418	22	5.3
Nonwhite				
All patients	158	316	13	4.1
Patients without associated defects	133	266	11	4.1
Patients without maternal complications	58	116	5	4.3
Patients not born prematurely	105	210	9	4.3

* Associated defects include cerebral palsy, mental deficiency, and malformations.

neonatal deaths, and a sublethal component consisting of cerebral palsy.[8] The results of this study suggest that this sublethal component should also include epilepsy. It is of additional interest that the association of these factors with epilepsy is not as great as with cerebral palsy. This observation, together with the fact that approximately one-third of persons with cerebral palsy have convulsive seizures, suggest that cerebral palsy may be a result of a more severe type of brain damage than is epilepsy. The results are sufficiently suggestive to warrant the continuance of similar studies concerning other possible components of this continuum. They also warrant giving serious consideration to the possibilities of establishing concurrent studies in which a group of infants classified by these maternal and fetal factors could be followed, so that one can actually measure the risks of various neurological conditions associated with these maternal and fetal factors developing.

In view of the existence of the association of the factors studied with epilepsy it is of interest to reexamine some of the data on which the genetic hypothesis is based. In addition to the questionable results discussed earlier in this report, there are two types of observations from which this hypothesis has been inferred. One consists of the observation that there exists familial aggregation in the case of epilepsy. Several investigators have reported that among siblings and parents of epileptics there exists a higher prevalence of epilepsy than is found in the general population.[9] This evidence has not been completely corroborated since in a recent report from Sweden, no increased prevalence was found.[10] In evaluating this evidence as indicating a genetic effect, it is necessary to remember that prematurity also shows familial aggregation. Karn and others indicated that once a premature birth occurs in a family, the risk of an additional premature birth is increased approximately threefold.[11] This might be a partial explanation of the increased prevalence of epilepsy among siblings of a person with epilepsy. This does not explain the finding of an increased prevalence of epilepsy among parents of persons with epilepsy, since there are no data indicating that prematurely born parents have an increased risk of having premature offspring. However, if the hypothesis that exogenous factors such as nutrition are causative in prematurity is substantiated, it is conceivable that similar environmental factors could be present with regard to both parents and offspring. Consequently, a possible explanation for the finding of familial aggregation in epilepsy is that it may be merely a manifestation of the familial aggregation of various maternal and fetal factors. At least it is evident that in any family studies of epilepsy these maternal and fetal factors must be taken into account in the analysis before any other inferences are derived.

A genetic hypothesis has also been inferred from twin studies. In these it has been found that the percentage of concordant twins is higher among monozygotic pairs than among dizygotic pairs. In evaluating this type of evidence it is of importance to take into consideration the differences that may exist between monozygotic and dizygotic twins with regard to maternal and fetal factors. An indication that such differences do exist has been presented by Yerushalmy and Sheerar, who found that there were more premature births of monozygotic pairs than dizygotic pairs.[12] They also found this same type of difference with regard to stillbirths. Unfortunately, no evidence exists as to whether or not this is also true with regard to other factors such as complications of pregnancy and delivery. It is thus possible that the twin differences with regard to prenatal and paranatal factors may account, completely or in part, for the observations made on twins in the case of epilepsy.

It is evident from these and similar observations referred to in this report that the hypothesis of the continuum of reproductive casualty provides a conceptual framework for investigation, since it does focus attention on an area within which lies the possibility of prevention of these neuropsychiatric disorders. It indicates the need for extensive studies of the factors causative to or associated with the complications of pregnancy and labor, since these not only influence maternal health and infant loss but appear to have an influence on the surviving infant. Any effort towards the prevention of the components of this continuum must of necessity be directed at an improvement in conditions associated with maternal health.

SUMMARY

The prenatal and paranatal records of 564 epileptic children born in Baltimore between 1935 and 1952 showed significantly more complications of pregnancy and delivery, prematurity, and abnormal neonatal conditions than a similar number of matched controls. These abnormalities were just as frequent among epileptic children whose parents did or did not have epilepsy. These epidemiological findings throw some light on the etiology of epilepsy and raise doubts as to the genetic basis of convulsive disorders. The continuum of reproductive casualty composed of a lethal component consisting of abortions, stillbirths, and neonatal deaths and a sublethal component consisting of cerebral palsy, epilepsy, and perhaps other conditions, is discussed with its implications for the etiology and prevention of certain neuropsychiatric disorders.

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BMR Tracings.—The respiratory tracing from which the basal metabolic rate is determined is seldom, if ever, inspected or analyzed by physicians. If these tracings were inspected, they would be of great value in obtaining information on pulmonary ventilation in thyroid dysfunction as well as in evaluating the state of the patient during the metabolism test. Apprehension, anxiety, and discomfort will appear as a grossly irregular tidal exchange, producing a variable oxygen uptake, sighing respirations, and a variation in the respiratory rate. The calculation of the tidal volume, respiratory rate, and minute volume will provide information of ventilatory activity relative to oxygen consumption.—Capt. J. C. Syner, Ventilation and Oxygen Absorption in Thyroidism, *United States Armed Forces Medical Journal*, April, 1954.

EFFECT OF TEA ON GASTRIC SECRETIONS AND MOTILITY

C. Wilmer Wirts, M.D., Martin E. Rehfuss, M.D., William J. Snape, M.D.
and
Paul C. Swenson, M.D., Philadelphia

Tea was probably used first in China, since there are accounts from visitors to that land in 850 A.D. describing the use of a medicinal beverage named "Chah" or "Fah." In Europe the use of tea as a beverage dates from the 17th century. The importance of this item in the diet can be gained from the fact that the annual consumption of tea in the United States now amounts to about 98,000,000 pounds per year.[1] In spite of the widespread use of this beverage, information regarding its physiological activity is limited. Psychological testing has shown that a cup of tea affords an immediate as well as a delayed lift without inducing secondary depressing effects.[2] This study was undertaken to investigate by objective methods the effects of tea on digestion and on various associated physiological processes.

In addition to caffeine and tannin, tea contains a variety of substances in small amounts; this includes minute quantities of volatile oils, certain trace elements and B vitamins, water soluble derivatives of tannin, chlorophyll, proteins and various carbohydrates. The effects of tea generally have been ascribed to its caffeine and tannin content, but reliable information on the effect of tea tannin is limited. It is often assumed that tea tannin behaves in the gastrointestinal tract just as the ordinary tannin of pharmacy or the tannic acid of the pharmacopeia does. The latter will combine with and precipitate proteins and gelatin and act as an astringent, a tanning agent, and inactivator of pepsin. Pseudotannins, which make up a considerable portion of tea tannin, have a feeble action in this regard.[3] It has been reported that tea tannin, being closely related to eriodicytol, possesses vitamin P activity.[4] It is probably because tannin is so often erroneously considered synonymous with tannic acid that textbooks state that large amounts of tea may exert a deleterious effect on digestion by precipitating proteins and albuminoses and thereby lessening absorption and irritating the gastric mucosa. According to a report from the Lancet Laboratory,[5] in tea we may be dealing with a combination of caffeine and tannin in the ratio of 1:3; on this premise, neither tannin nor caffeine would be present in the free state in the stomach in sufficient amounts to exert the deleterious effects that both might independently possess. A study by Halpenny and MacDermot [6] serves to illustrate the harmfulness of tannic acid of the pharmacopeia and caffeine when administered alone and the absence of such effects after the use of tea. Constipation, nausea, and in some instances vomiting occurred after the second dose of either 5 grains (0.32 gm.) of tannic acid or 2.5 grains (0.16 gm.) of caffeine alone. Tannic acid combined with caffeine produced fewer and less marked disturbances; with the use of tea prepared in the usual fashion and taken in average amounts of two cups, gastrointestinal disturbances did not occur in any subject.

Of the investigators who have attempted to evaluate the influence of tea on digestion, very few have studied the effects on gastric emptying. Miller, Bergheim, Rehfuss, and Hawk [7] found that the evacuation of the stomach was not appreciably delayed by the drinking of excessive quantities of beverages such as one liter of iced water, iced or hot tea, or hot coffee (either plain, with cream, or with sugar and cream). The addition of sugar alone to coffee delayed gastric evacuation.

MATERIALS AND METHODS

The present study was undertaken for the purpose of determining the effect of tea on digestion in general and evaluating, if possible, the mechanism by which it leads to the relief of simple postprandial distress. We were especially anxious to learn the effect of tea taken in average amounts and as it is customarily prepared for the average tea drinker. Therefore the tea was prepared according to the directions on the label of commercially available tea bags,[8] steeping one bag (average tea content, 2.3 gm.) per cup (150 cc.) of boiling water for three minutes. By chemical analysis this was shown to yield 0.03 to 0.032 gm. per 100 cc. of crude caffeine, or approximately 45 mg. (0.75 grain) per cup.[9]

The amounts of tea and water used as a beverage throughout this study were always 300 cc. unless otherwise noted. We considered this amount to approximate two cups and to represent the amount consumed by the average person at any one time. Because the majority of people take sugar in tea, 10 gm. of sugar were added to every 300 cc. of tea or water used. This small amount of sugar produced no demonstrable effect, since in each group of studies a control without sugar failed to show any significant difference in the results. When hot beverages were given they were between 55 C and 60 C; iced beverages were at 5 C.

The first phase of the work constituting the basis of this report deals with the effect of tea on the pH and pepsin of gastric secretion and on gastric motility. Additional work is in progress dealing with biliary and pancreatic secretion and the comparative effects of tea with caffeine and decaffeinated tea. The subjects studied were patients attending the gastrointestinal outpatient clinic of the Jefferson Hospital. Over 300 intubation studies were performed in 114 persons during an 18 month period. Each of these subjects had been attending the clinic for a sufficient period to permit thorough investigation and were diagnosed as having either inactive duodenal ulcer or functional gastrointestinal disorder. A few patients who had achlorhydria not associated with other demonstrable disease were also studied. To serve as a control it was decided to compare the effect of tea to that of water under

From the departments of medicine and radiology and the therapeutic laboratories of the Jefferson Medical College and Hospital.

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identical circumstances, and therefore each test was repeated on the same patient on a different day substituting water for tea.

The effect of tea and of water on the pH and pepsin of gastric juice obtained from fasting subjects was determined in vitro. The effect of tea and water on the pH, pepsin, and gastric emptying time with and without various types of meals was made following fractional gastric aspirations; subsequently gastric motility was also studied by an intragastric balloon technique and roentgenologic observation. Pepsin determinations were made according to the Riggs-Stadie method [10]; pH values were read on a Beckman pH meter using a glass electrode; free acid was titrated with dimethyl-amino-azobenzene (Töpfer's reagent) and total acid with phenolphthalein. Free and total acid were expressed as clinical units.

To facilitate aspiration, liquid meals of fat, protein, or carbohydrate were given through a gastric tube passed just prior to the test. To determine the type of meal that would serve as a practical guide, 75 patients without demonstrable organic gastrointestinal disease were studied by administering through a gastric tube varying amounts of tap water, as well as saline, fat, carbohydrate, and protein solutions. The fat used was olive oil emulsified with polyoxyethylene (20) sorbitan mono-oleate (Tween 80), the protein was Bacto-peptone, and the carbohydrate was granulated sugar. The solutions and emulsion were given in varying concentrations of 5, 10, 20, and 40%. We found the tap water, saline solution, and tea all left the stomach at about the same rate (almost completely in 30 minutes), but that fat, carbohydrate, and peptone were delayed approximately in proportion to the concentration of the solution or emulsion used.[11] The 40% concentrations gave the greatest delay in emptying without blocking the stomach tube during the injection or aspiration. This concentration was therefore selected as the one that would magnify the effect of tea on the gastric emptying when compared with the effect of an equal quantity of water.

TABLE 1.—*In Vitro Effect of Adding Tea or Water to Gastric Juice (Averages for Ten Trials)*

	Free Hydrochloric Acid, Clinical Units	Total Acid,* Clinical Units	Pepsin K-Factor	pH
Gastric juice	54.4	74.5	0.189	1.3
Gastric juice plus tea (1:4)	13.1	22.8	0.069	1.9
Gastric juice plus water (1:4)	13.7	20.0	0.093	1.8

* Averages for 6 trials.

TABLE 2.—*Effect of Three Hundred Cubic Centimeters of Tea or Water at 60 C on Gastric Secretion (Averages for Twelve Subjects)*

	Fasting	After 30 Min.	After 60 Min.	After 90 Min.	After 120 Min.
Free Hydrochloric Acid, Clinical Units					
After tea	17.7	25.1	36.9	36.2	23.4
After water	6.7	19.1	21.0	24.7	19.3
pH Value					
After tea	2.1	1.9	1.7	1.8	1.9
After water	2.5	1.9	1.9	1.9	1.8
Pepsin (K-Factor)					
After tea	.101		.148		.113
After water	.104		.170		.189

RESULTS

In Vitro Study.—To determine the direct effect of tea and water on gastric juice in vitro, 75 cc. of hot tea, prepared in the usual manner for this study, was added to 25 cc. of gastric juice and allowed to stand 30 minutes at room temperature before redetermining the free and total acid, pepsin, and pH value. The procedure was then repeated using hot water instead of tea. The gastric juice was obtained from 10 subjects without gastric disease following histamine stimulation.

As shown in table 1, the difference in the effect (average figures from 10 tests) of hot sweetened tea or water on free and total acid, pepsin, and pH of gastric juice in vitro is not great and probably represents one of dilution, although a buffering effect may be present. There was no evidence of precipitation or flocculation.

Gastric Secretion in Ulcer Patients.—To determine the effect of tea alone on gastric secretion and motility, 12 subjects were given two cups of hot tea (300 cc. at 60 C with 10 gm. of sugar). This was administered through a gastric tube after testing the fasting residue for volume, bile content, pH, and free acid. Thereafter samples were similarly tested at 30, 60, 90, and 120 minutes. Only a small sample of the gastric aspirate was retained for chemical studies at the end of each of these 30 minute periods; the remainder was reinjected into the stomach. Twelve of the same subjects were then restudied; we replaced the hot tea with an equal amount of hot water. All of the subjects in this group had duodenal ulcer in a state of remission. They were purposely selected because it was thought they would show the greatest response to any gastric secretory stimulus.

Because of the voluminous data the results are given as average values. As shown in table 2, there is little difference in pH but the free acid is somewhat higher after the administration of tea than water. Pepsin values at one hour and two hours after the patient was given tea are somewhat less than after the patient was given water. It is doubtful if the rather small difference in acid levels is significant, if the average values in the fasting residue of those subjects receiving tea are compared with those receiving water. So far as the gastric emptying for both beverages is concerned, the bulk of the administered material left the stomach at 30 minutes. Regurgitated bile was observed in the stomach only rarely.

Gastric Emptying After a Fat Meal.—After removing the fasting residue and testing it for volume, bile, pH, pepsin, and trypsin, a fat meal (250 cc. of 40% emulsified olive oil) was given with two cups of hot tea to 20 subjects. The stomach was emptied at one-half hour intervals for two hours, and after the volume was measured the material was reintroduced into the stomach, only a small sample being kept for testing the pH, bile, pepsin, and trypsin. Each of the subjects had the test repeated on a different day, and an equal quantity of hot water was substituted for the tea. These studies were repeated on 12 subjects in an identical fashion with iced tea and iced water.

Trypsin was never found and bile was rarely found in the aspirated material. No significant difference was noted in the pH, free acid, and pepsin between the tea

and water, but there was a difference in emptying time, which was shorter with tea than water and with cold rather than hot beverages. The amount of this fat meal that left the stomach in 30 minutes with the two beverages at different temperatures is compared with other types of meals in figure 1. In figure 2 the average volumes for gastric residue at 30-minute intervals for the entire two hour period are represented graphically.

Gastric Emptying After a Peptone Meal.—Tests were repeated in the same fashion as for the fat meal, except that on this occasion a 40% peptone meal was used. Increased gastric emptying was noted when hot and iced tea was given in comparison to hot and iced water. The increase following hot tea is not great until after the 60 minute period.

Gastric Emptying After a Carbohydrate Meal.—Ten subjects were investigated in a fashion similar to those who received the fat meal with hot tea and water, except that a 40% carbohydrate meal replaced the fat. Eight subjects received the beverages iced. An increased rate of emptying following hot and iced tea occurred at all intervals except at 30 minutes.

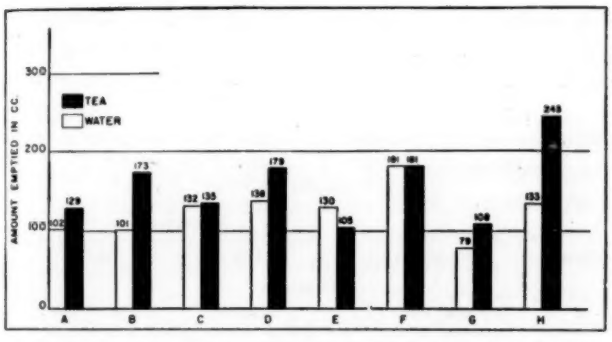

Fig. 1.—Average amount emptied from the stomach 30 minutes after the ingestion of various meals taken with tea or water. The amount of liquid given was 300 cc., and the amount of the meal given was 250 cc. *A*, liquid at 60 C, 40% fat meal (20 subjects). *B*, liquid at 5 C, 40% fat meal (12 subjects). *C*, liquid at 60 C, 40% protein meal (17 subjects). *D*, liquid at 5 C, 40% protein meal (4 subjects). *E*, liquid at 60 C, 40% carbohydrate meal (10 subjects). *F*, liquid at 5 C, 40% carbohydrate meal (8 subjects). *G*, liquid at 60 C, eggnog type meal (2 subjects). *H*, liquid at 5 C, eggnog type meal (5 subjects).

Gastric Emptying After a Combined Meal of Fat, Protein, and Carbohydrate.—In order to test the effect of a combined meal, an eggnog was prepared by mixing one pint (500 cc.) of milk, two eggs, one tablespoonful (8 cc.) of sugar and a teaspoonful of vanilla. This was administered to two of the subjects in 250 cc. amounts with hot tea or hot water. The same type of 30 minute aspirations and determinations were made for a two hour period as in the fat meal study. The eggnog meal was then given to five additional subjects when the beverages were iced. An increased rate of emptying was noted with hot and iced tea when compared with hot and iced water at all intervals.

Gastric Emptying After a Fat Meal Studied Fluoroscopically.—To avoid the effects of prolonged gastric intubation, a barium meal in addition to fat and tea was administered to 16 subjects. The emptying of the barium from the stomach was then studied fluoroscopically. The following material was given through a gastric tube: 100 cc. of barium suspension, 250 cc. of 40% emulsified olive oil, and 300 cc. of hot tea. The gastric tube was then withdrawn and the subject observed fluoroscopically at intervals until complete emptying of the stomach had taken place. The test was then repeated on a subsequent day in the same subject; the tea was replaced with water. Thirteen of the subjects were given hot beverages, and the test was performed on three subjects with iced tea and iced water.

The response to this procedure is shown in table 3. It should be noted that one subject was tested with a protein meal and one with an eggnog meal. In 11 out of 13 subjects who received both hot tea and hot water following the fat, protein or eggnog meal, the stomach emptied up to 2 hours and 45 minutes sooner with tea than with water. In only two instances was the emptying time

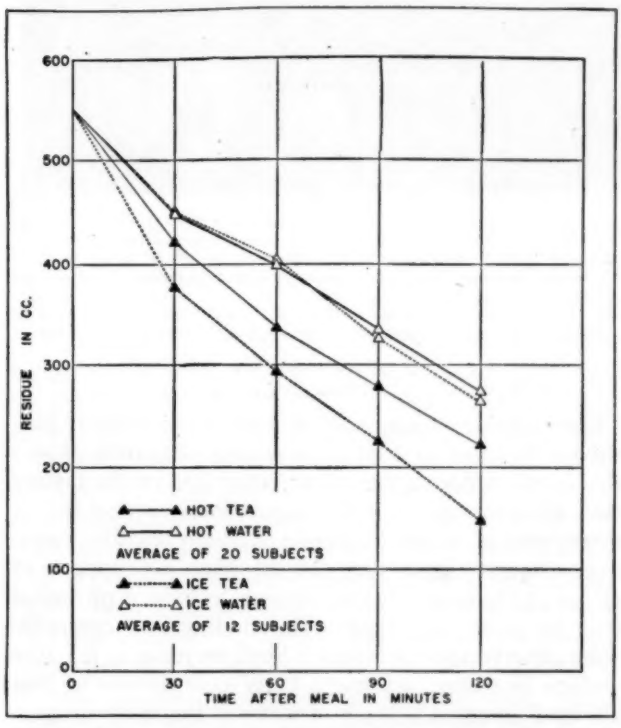

Fig. 2.—Effect of tea and water on gastric emptying after a 40% fat meal. The amount of hot liquid given was 300 cc. (at 60 C), and the amount of the 40% fat meal was 250 cc. The fasting residues for the hot liquid and meal were 20 cc. and 19 cc. The amount of cold liquid given was 300 cc. (at 5 C), and the amount of the 40% fat meal was 250 cc. The fasting residues for the cold liquid and meal were 18 cc. and 18 cc.

shorter after water was given than after tea; in one the difference was 40 and in another 45 minutes. When the results are averaged in minutes they are as follows: The average emptying time in 13 trials with hot tea (60 C) was 266 minutes and with hot water 327 minutes. The average time in 3 trials with iced tea (5 C) was 193 minutes, and with iced water 250 minutes.

Gastric Activity Studied by Intragastric Balloon.—Gastric activity was studied in four subjects by employing a gastric balloon and recording motility on a kymograph. After a basal tracing the fasting subject drank 240 cc. of hot tea, and a record was then made to observe the effects on gastric movement. On a subsequent day the test was repeated substituting hot water for the tea. Figure 3*A* shows the kymograph tracing indicating the

increased gastric motility following the administration of hot tea. The usual complete obliteration of motility following the administration of water was observed in subject A, and a simultaneous tracing in subject B shows the increased motility after the administration of tea, (fig. 3*B*).

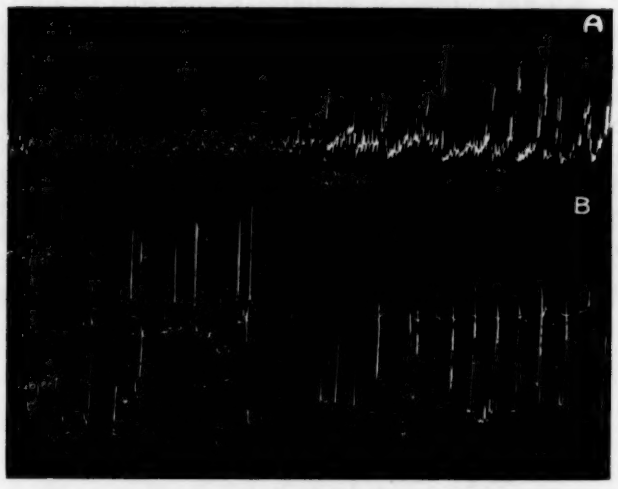

Fig. 3.—*A*, tracing of gastric motility using an intragastric balloon in a fasting adult subject. A prompt increase in motility occurred immediately and lasted 20 to 30 minutes after the subject drank 240 cc. of tea at 60 C with 10 gm. of sugar. *B*, tracing of subject A shows obliteration of gastric peristalsis after the subject drank 240 cc. of water at 60 C with 10 gm. sugar. Tracing of subject B shows increased gastric motility after a brief period after the subject drank 240 cc. of tea at 60 C with 10 gm. of sugar.

COMMENT

From these data it appears that tea as customarily prepared with sugar and taken in average amounts of two cups is not a potent gastric secretagogue in the fasting state. Data not given in this report indicate that this is equally true in the postcibal state. Actually tea, like water, when taken by a fasting subject does not appear to remain in the stomach long enough to have a profound effect on gastric secretions. This finding is comparable to the observations of others.[12] Such increase as tea may produce in gastric acidity is fairly comparable to that following an equal amount of water at the same temperature. An examination of the data reported by Roth, Ivy, and Atkinson [12c] tends to support this. Following the administration of tea there is somewhat less pepsin present in the gastric secretion than when water is given, but it is doubtful whether this difference is of sufficient magnitude to be significant. The reduction in acid and pepsin value following the addition of tea to gastric juice in vitro appears to be primarily due to a dilution factor and is quite comparable to the effect of an equal amount of water.

Of fairly consistent occurrence was the moderate but definitely increased rate of gastric emptying of various meals when tea was given in comparison to water. Temperature also appeared to play a role, inasmuch as iced beverages produce a more rapid emptying than hot. This corresponds to the report of Gershon-Cohen, Shay, and Fels [13] who gave barium suspended in 250 cc. of a 2% solution of Liebig's extract and found that the colder the meal, the greater the rate of gastric evacuation; later Weintraub and Williams [14] demonstrated that iced saline solution given after a barium-saline meal produced a marked acceleration of the barium through the small intestine. In our study the increased rate of emptying after the administration of hot and iced tea was established also by fluoroscopic studies, and increase in gastric tone and motility was demonstrated by the intragastric balloon technique with hot tea.

It is generally held that the distress so frequently noted after taking a heavy meal is associated with decreased gastric tone and motility and at times reversed peristalsis.[15] Since tea increases gastric tone and the rate of gastric emptying, it would appear that such postprandial relief as it produces is brought about by its effect on the gastric musculature. Furthermore, since it has been shown that increased gastric emptying is associated with increased motility of the small intestine as well as the flow of biliary and pancreatic juice and intestinal juice, it might be inferred that such stimulation follows the ingestion of tea.[16] Excessive stimulation of this type that conceivably might follow an iced meal does not seem to occur with hot tea. Consequently, within the limits of this study it is felt that the long-held belief that a cup or two of tea with meals has value in aiding digestion and relieving postprandial distress is justified.

It would be of considerable interest to determine which factor or factors in tea is responsible for this. There is no evidence as yet that the caffeine or tannin in tea has any specific effect in this regard. Although caffeine influences the action of the myocardium and the smooth muscle of blood vessels and bronchi, it is stated that it has no effect on the gastrointestinal system in man.[17] As we mentioned earlier in this paper, tea tannins are quite different from tannic acid; in fact, the difficulty in obtaining them separately in sufficient quantity for study has been so great that little concise data on their action is available. The mechanism of gastric emptying

TABLE 3.—*Gastric Emptying Observed Fluoroscopically After the Administration of Tea and Water with a Fat Meal and Barium*

Subject	Diagnosis	Emptying Time	
		Tea	Water
	Liquid at 60 C		
1	Duodenal ulcer	6 hr. 25 min.	5 hr. 45 min.
2	Duodenal ulcer	3 hr.	5 hr. 45 min.
3	Duodenal ulcer	4 hr. 10 min.	4 hr. 20 min.
4	Duodenal ulcer	4 hr. 10 min.	6 hr.
5	Functional gastrointestinal disorder	4 hr. 45 min.	6 hr.
6	Duodenal ulcer	3 hr. 10 min.	3 hr. 15 min.
7	Functional gastrointestinal disorder	4 hr. 45 min.	4 hr. 55 min.
8	Duodenal ulcer	2 hr. 30 min.	5 hr.
9	Functional gastrointestinal disorder	3 hr.	3 hr. 15 min.
10	Duodenal ulcer	7 hr. 30 min.	8 hr. 30 min.
11	Functional gastrointestinal disorder	8 hr.	10 hr.
12	Duodenal ulcer	3 hr. 30 min.	6 hr.
13	Functional gastrointestinal disorder	2 hr. 45 min.	2 hr.
	Liquid at 5 C		
14	Functional gastrointestinal disorder	2 hr. 40 min.	3 hr.
15	Functional gastrointestinal disorder	3 hr.	4 hr.
16	Functional gastrointestinal disorder	4 hr.	5 hr. 30 min.

* Three hundred cubic centimeters of water were given with a fat meal consisting of 250 cc. of 40% emulsified olive oil. Subjects 12 and 13 were given protein and eggnog meals, respectively.

has been extensively investigated ever since the pioneer observations of Beaumont, and while opinion is not uniform, it is now generally believed that the tone and motility of the antrum, the consistency and osmotic pressure of the gastric contents, and the contents of the duodenum all influence the rate of gastric emptying.[18] Probably to this should be added the influence of the temperature of the gastric contents. Also it has been shown that 100 cc. to 400 cc. of water will decrease the gastric emptying time for solid foods.[19] This effect must be brought about by the fluid volume of tea but does not represent the whole mechanism, because the decrease in emptying time was greater with tea than in the control studies with water and with iced beverages in comparison to hot. To adequately explain the mechanism whereby tea increases the rate of gastric emptying requires further investigation, but its influence on the gastric musculature is probably one of the important factors.

CONCLUSIONS

1. Tea appears to increase the rate of gastric emptying when compared to the effect of an equal amount of water, when used with a 40% protein, carbohydrate, fat, or combined (eggnog) meal. 2. The iced beverages used have a more pronounced effect in this regard than hot. 3. Tea appears to stimulate gastric motility. This is apparent from the investigation of the amount of gastric residue remaining after various meals with tea and water, both by tube and fluoroscopy as well as by the use of the intragastric balloon with the beverages alone. 4. Tea, when compared to the effect of an equal amount of water, exerts approximately the same effect on the gastric secretory output (volume, pH, free acid, and pepsin). 5. These data suggest that the use of tea, taken as a beverage in average amounts, need not be contraindicated in the treatment of most gastrointestinal conditions.

THE THUMB AS A CLINICAL AID IN DIAGNOSTIC SCREENING OF PARALYSIS

Temple Fay, M.D., Philadelphia

The opposability of the thumb to the finger tips is one of the unique attributes that distinguishes man from all other primates and mammals. The normal human infant is born with the thumb flexed into the palm. This position is more or less retained until the third or fourth month of postnatal life. Voluntary grasping movements then arise to individualize the thumb's activity. The thumb maintains a larger cortical representation in the motor area of the cortex than the other digits. It is extremely sensitive to functional disturbance and therefore of great value in differentiating between the various types of paralysis that involve the nervous system from the brain to the upper extremity.

Patients who have recovered from the acute manifestations of a neurological lesion above the midcervical level usually display characteristic alteration of the thumb position and may readily be screened into groups for special studies or indicated dispensary, clinic, ward, or hospital assignment.

If the clinician will study carefully the position of the thumb in normal persons who are unaware of the scrutiny it will be noted that the thumb lies in a plane approximately at right angles to the dorsum of the hand and is characteristically separated from the fingers and the palm. Once the normal thumb position has been recognized, as well as its relation to the hand and wrist during the associated movement of walking (the upper extremity swings forward slightly and just prior to the advancing lower extremity of the opposite side), it will be possible to detect certain types of paralysis as the patient walks into the examiner's room; or if paralysis is present, a few rapid tests of the thumb may determine if the lesion involves the brain, cord, brachial plexus, or peripheral nervous structures. When rapid neurological screening of patients is required the following tests are sufficiently accurate to serve as a guide to the examiner as to the probable area of involvement and the level of the lesion.

The majority of neurological diseases and dysfunctions are named after their anatomic and supposed pathological processes (viz., anterior poliomyelitis, posterolateral sclerosis) or functional alterations (viz., spastic diplegia, lenticulostriate dystonia, decerebrate rigidity). It is extremely helpful to localize the lesion or process as to anatomic level, knowing certain pathological processes characteristically involve these areas. A careful detailed history is as important as a careful neurological examination. With a careful chronological history and a rapid screening survey, a high degree of accuracy of initial diagnosis can be attained.

Where symptoms and signs indicate diffuse involvement of the nervous structure (encephalitis, multiple sclerosis, meningitis, arteriosclerosis, etc.), these diagnoses may be permissible as tentative classifications, requiring later on more than ordinary review of the history and clinical findings with detailed examination of the patient. Procedures that tend toward more definite localization of a lesion often lead to a more specific diagnosis and consequent appropriate and specialized treatment.

During routine physical examinations of supposedly neurologically normal students, workers, or patients, an abnormal thumb position and associated Hoffmann sign have been detected on a small but significant number. Detailed searching of the history has almost invariably shown either organic lesions unsuspected by the patient or serious central nervous system involvement (trauma, meningitis, convulsions) in the past. Careful noting of the thumb position and the following tests I have found of great clinical value as a clue to diagnosis.

Cortical Thumb.—If the thumb tends to remain flexed at the tip or is drawn into the palm (fig. 1), the clinician

may suspect an oncoming, existing, or a recovery phase of cortical spastic paralysis (upper motor neurone involvement). Obviously, the thumb position must not be due to deformity, ankalosis, or contracture.

Flaccid types of cortical paralysis may at first glance resemble cord or root involvement. Careful history and neurological examination will be required if only the

Fig. 1.—Thumb flexed and drawn into the palm in partial or oncoming spastic types of paralysis.

hand and arm are involved (monoplegia). Here examination of the thumb and hand may be of great value in that cord and root lesions show characteristic atrophy of the intrinsic muscles similar to that seen in figure 2.

In spastic children who are sitting or walking, the hand (thumb pointing downward) is carried out and away from the body. In the adult it is flexed at the wrist (fig. 3) and usually drawn by flexion of the forearm toward the chest. A Hoffmann sign should be present.

A lesion involving the pyramidal tracts (spastic type of paralysis) may be present at any point above the fifth cervical segment of the cord (fig. 4) to the surface of the brain, but as the majority of lesions involve the upper levels, particularly the cerebral hemisphere, the term cortical thumb has been adopted to suggest the probable site of the pathological conditions within the hand area. If there is no involvement of the lower two-thirds of the face (seventh cranial nerve) or the lateral movement of the eyes (sixth cranial nerve) the chances are the lesion lies between the mastoid level (medulla) and the mid-neck (upper cervical cord). Roentgenograms for subluxation of the atlas or special myelographic studies of the high cervical area may be indicated. Sensory studies for accurate localization of a lesion should also be undertaken.

Midbrain Thumb.—In patients with deep-seated central brain pathological conditions such as the Parkinsonian types (rigidity) where the so-called extrapyramidal system is involved (basal ganglions), the patient usually cannot rapidly and repeatedly touch the tip of the thumb to the tip of the index or middle finger. The movement is slow, stiff, and delayed. In rigidities the components of movement are present, but they are deliberate and slow. In true motor paralysis or weakness the movement or portions of movement are feeble, uncertain, or absent. Free swinging of the arm (associated movement) and hand coordination in walking is absent.

With this quick simple test the clinician may be alerted to pathological conditions situated within the deep structures of the brain (inflammation, encephalitis, focal lesions of the basal ganglions, degenerations causing rigidity, dystonia, and postencephalitic Parkinsonian syndromes).

Cerebellar Thumb.—With the patient standing (if possible) and the arms extended horizontally to the side, fingers and thumb wide apart, the physician requests the patient to touch the tip of the thumb to the tip of the nose with the eyes closed. This procedure has often been too well practiced (by some patients in childhood for other purposes) and the index finger may be required as a substitute. An intention tremor (diffuse lesions like multiple

Fig. 2.—Atrophy of the intrinsic muscles of the hand owing to spinal cord or root involvement. The patient can place the tip of the thumb over and in back of the knuckle of the index finger.

sclerosis) or definite dysmetria (cerebellar-vestibular ataxia) may be quickly detected. Fine midbrain types of tremors tend to disappear with this movement, thyroid and functional tremors persist. Malingerers will, among other things, enjoy exaggerating deliberate inaccuracies.

If after careful instruction the patient misses the proper contact point (tip to tip) on the first trial but makes a

successful correction on the second (particularly if the disturbance is unilateral), an intrinsic cerebellar dysfunction should be suspected and further confirmation sought in appropriate cerebellar-vestibular studies. A cooperative, normal 4-year-old child can do this test on the first attempt; a cerebellar tumor patient cannot.

The cerebellar patient, with eyes closed, usually tends to fall to the side of the lesion, or backward, while persons with ataxia of the kinesthetic types (sensory) sway and lurch and manifest a typical Romberg response.

The presence of a pendular or a diminished patellar reflex response may be further confirmation of the cerebellar types of ataxia. The kinesthetic (sensory) types of ataxia are characterized by persistent dysmetria, intention tremor, and incoordination. Movements are jerky, and walking with eyes closed is difficult. Mixed vestibular-cerebellar-sensory involvement (diffuse lesions of the posterior fossa) are associated with additional disturbances in ocular movement, gait, speech, and posture.

Fig. 3.—Hand of patient with chronic spastic paralysis. The thumb is drawn firmly into the palm, and the fingers close over the thumb with contractions of the flexors of the wrist.

Cord Thumb.—When the spinal cord is directly involved by a lesion (myelitis), or around its roots (sixth, seventh, and eighth cervical nerves for hand) there occurs atrophy, or weakness, of the intrinsic muscles so as to permit the tip of the thumb to be placed completely back of the knuckle of the index finger (fig. 2). "Double jointed" persons can almost assume this position, but cannot do so without force. The deep tendon reflexes are lost and muscle tone absent. Where weakness with atrophy occurs without sensory change, myelitis or root involvement (neuronitis) may be suspected. If sensory changes are of segmental (cord or root dermatomere pattern) they denote lesions or pressure involving both sensory and motor modalities, probably localized in the cervical area.

Where pure motor signs prevail the clinician may suspect anterior poliomyelitis, amyotrophic lateral sclerosis, syringomyelia, or local or focal intrinsic lesions of the cord (hematomyelia) and roots. Proper confirmatory studies may then be arranged.

Musculospiral (Radial) Thumb.—In paralysis of the musculospiral or radial nerve the thumb cannot be cocked backward or held against resistance as in figure 5. The sensory change is on the dorsum of the hand around the base of the thumb and adjoining fingers.

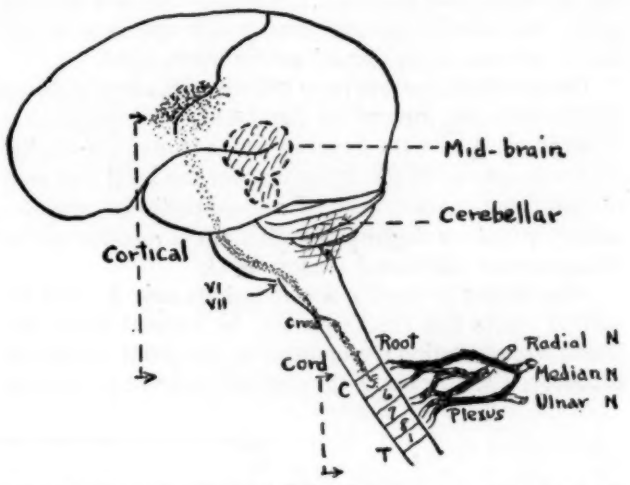

Fig. 4.—Schematic guide to levels of involvement as indicated by the thumb tests in various types of paralysis.

Median Thumb.—Median nerve paralysis makes it impossible for the thumb to be tightly held against the side of the index finger (this is partly an indirect effect but still a good median nerve test in rapid screening procedures). Typical median nerve sensory disturbance in the palm and base of the middle and index finger is present.

Fig. 5.—Diagram of cocked-up position of the thumb that patient with radial or musculospiral paralysis cannot maintain.

Ulnar Thumb.—Ulnar nerve paralysis makes it impossible for the thumb to touch the tip of the little finger across the palm. The sensory defect is characteristic to the ulnar nerve skin distribution.

Plexus Thumb.—A flaccid type of paralysis is present and the thumb cannot be moved to (1) touch the tip of the fingers, (2) be held to the side of the index finger, or (3) be cocked backward in extension as in figure 5. There is usually a combined sensory and vasomotor defect as well. The paralysis is profound, and skin, reflex, tone, and vasomotor facilities are profoundly altered throughout the hand and forearm. Lesions in the arm pit and under the clavicle or root emergence openings in the lateral cervical spine should not be overlooked.

The peripheral nerves have individual sensory patterns and if they are injured or paralyzed, light percussion (Tinel's sign) with the finger or reflex hammer along the anatomic course of the nerve or over the level and area of suspected involvement, if not palpable or obvious, usually produces tingling and discomfort referred to the characteristic peripheral sensory field.

After injury or focal intrinsic lesions have existed for several weeks the Tinel sign may be noticed below the lesion (regeneration) and used as an index of partial recovery. The absence of the sign will indicate prevention of the return of nerve fiber growth below the level of the lesion, probably caused by scar tissue or neuroma. More detailed studies may then be planned for the area, such as electrical reactions and sensory and vasomotor tests.

This entire series of thumb tests requires only a few minutes to accomplish after the examiner has become familiar with the normal and abnormal types. Inspection and examination of the patient in greater detail is indicated and should be instituted when thumb deviations occur.

The thumb tests noted above have proved a satisfactory screening guide to the probable character and location of lesions (brain, cord, or peripheral nerve) when weakness or paralysis of the upper extremity and the hand has occurred or been observed. Rapid screening of patients in routine physical examinations makes possible selection of those requiring more detailed questioning, history, and studies focused on the involved area. The final neurological diagnosis will rest on completion of full clinical and laboratory studies.

8800 Germantown Ave.

TREATMENT OF HYPOTHYROIDISM WITH SODIUM LEVO-THYROXIN GIVEN ORALLY

Paul Starr, M.D.
and
Ruth Liebhold-Schueck, Los Angeles

The discovery of thyroxin in 1915 by Kendall and its subsequent synthesis in 1927 by Harington and Barger was followed by the use of this medicament in racemic form by the physicians of Europe and Latin America. The American physician has not used thyroxin extensively because of the report in 1939 that only a very large dosage was able to maintain the metabolism of the patient with myxedema.[1] These studies had led to the conclusion that thyroxin was relatively insoluble and was absorbed from the alimentary canal incompletely and irregularly.[2] This belief was contradicted in 1950 by the experience of Hart and Maclagan [3] who found that synthetic *l*-thyroxin given orally, produced by a new method, would correct myxedema in dosage as low as 0.3 mg. per day.

The modern material is synthetic sodium *l*-thyroxin, i. e., it is not a racemic mixture. Since 1950, a number of articles on the successful treatment of thyroid deficiency with this product have appeared.[4]

PREPARATION

In the last few years basic chemical studies have led to the elucidation of several commercially feasible methods for the synthetic preparation of thyroxin. In their synthesis, Hems and co-workers [5] use 3,5-dinitro-N-acetyl-*l*-tyrosine as a starting material. This compound is iodinated in aqueous solutions of primary or secondary aliphatic bases in the 3′, 5′ positions to yield *l*-thyroxin in approximately 25% over-all yield.

The direct formation of thyroxin from two molecules of 3,5-diiodo-tyrosine by an oxidative coupling reaction has been known for more than a decade, but yields by this approach have been prohibitively low from a commercial viewpoint. A group of investigators at Travenol Laboratories, Inc. has recently determined the novel conditions required to increase the yield of *l*-thyroxin obtained in this oxidative coupling reaction to many times the best yield yet reported in the literature, thus providing another practicable production method. As a result of these chemical production methods, synthetic thyroxin is now available at a price to the patient that is economical and comparable to that of desiccated thyroid.

From the thyroid clinic of the Los Angeles County Hospital and the Department of Medicine of the School of Medicine, University of Southern California.

The medicaments used in these studies were provided by Travenol Laboratories, Inc., a subsidiary of Baxter Laboratories, Inc., Morton Grove, Ill.

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MATERIAL AND METHODS

Patients of the thyroid clinic of the Los Angeles County Hospital who were found to have hypothyroidism were given sodium *l*-thyroxin orally and studied during some cases, for over two years. The pathological condition of the thyroid gland in relation to the causes of the hypothyroid state was determined by the effect of thyrotropic hormone administration on the radioactive iodine

TABLE 1.—*Effect of Sodium l-Thyroxin Given Orally on Spontaneous Hypothyroidism*

Case	Average Protein Bound Iodine Before Treatment, Mcg./100 Cc.	Medicament: Thyroid, Grains	Medicament: Thyroxin, Mg.	Laboratory Tests While Patient Received Maintenance Dose of Medicament (Average): Protein Bound Iodine, Mcg./100 Cc.	Cholesterol, Mg./100 Cc.	Basal Metabolic Rate, %	Total Time of Treatment, Months	Clinical Condition
1	3.4	..	0.8	4.9	242	+ 7	15	Diabetic; age 70+; died of cerebrovascular accident
2	1.2	..	0.7	5.6	...	— 9	21	Rehabilitated from unemployment to full time work
	1.2	..	1.0	10.2	...	+25	..	Toxic
3	0.9	1	...	1.4	309	....	7	Little improvement with desiccated thyroid
	0.9	..	0.2	5.9	297	....	25	Marked symptomatic improvement with thyroxin
4	1.0*	..	0.6	8.8	269	—19	12	Great improvement in hypothyroid condition; epileptic; hypertensive heart disease; died of cerebrovascular accident
5	1.0	..	0.4	8.4	258	—15	34	Late accumulation of thyroxin; basal metabolic rate +18%; protein bound iodine 10.9 mcg. per 100 cc.
	1.0	..	0.1	4.1	...	—13	7	Euthyroid
6	2.6	..	0.8	8.7	232	— 6	10	Some improvement
7	0.5	..	0.3	6.5	256	—13	12	Euthyroid
8	1.1	4	...	5.5	...	0	31	Was amenorrhagic 1½ yr. before treatment
	1.1	..	0.8	10.1	...	— 1	4	Normal menses now
9	1.4	..	0.1	4.2	274	....	6	Some improvement
10	2.4	..	0.4	6.8	225	— 8	6	Some improvement

* This patient had been given desiccated thyroid for many years before this protein bound iodine value was determined.

TABLE 2.—*Effect of Sodium l-Thyroxin Given Orally on Hypothyroidism Resulting from Treatment of Hyperthyroidism*

Case	Average Protein Bound Iodine Before Treatment, Mcg./100 Cc.	Medicament: Thyroid, Grains	Medicament: Thyroxin, Mg.	Laboratory Tests While Patient Received Maintenance Dose of Medicament (Average): Protein Bound Iodine, Mcg./100 Cc.	Cholesterol, Mg./100 Cc.	Basal Metabolic Rate, %	Total Time of Treatment, Months	Clinical Condition
11	2.5	2	...	4.7	270	....	24	Some improvement
	2.5	..	0.4	7.6	237	+ 4	24	Great improvement; working full time; married
	2.5	..	0.6	10.7	...	+24	..	Overdosage
12	2.7	..	0.8	7.3	240	—12	20	Some improvement
	...	..	1.0	8.4	...	....	..	Definite improvement
13	1.9	..	0.4	6.8	260	—10	6	Improved
14	1.4	..	0.8	...	...	+24	19	Became clinically toxic
	1.4	..	0.4	5.2	...	+ 9	..	Normal
15	1.0	..	0.4	5.1	176	—26	12	Definite improvement, but not yet euthyroid
16	2.8	3	...	6.7	...	—26	10	Minimal improvement
	2.8	..	0.4	8.1	216	—20	..	Some improvement
	2.8	..	0.8	8.0	169	— 7	22	Definite subjective improvement
16a	0.9	..	0.4	4.9	222	—11	16	Improved
17	1.4	..	0.6	8.0	246	—11	..	Great improvement initially; became clinically toxic on 0.6 mg.
				9.4	...	....	24	
	1.4	..	0.3	7.5	...	....	3	Nontoxic, well controlled
18	1.5	..	0.1	3.3	313	—20	4	Minimal improvement clinically. Electrocardiogram showed normal results after approximately 1 mo. medication
19	1.8	..	0.4	6.0	190	....	12	Menorrhagia much improved
20	3.6	..	0.4	7.6	145	—10	24	Good condition; normal pregnancy, but patient became toxic at end of second trimester. Last trimester off medication; delivery at term and normal lactation
21	1.5	4	...	6.6	216	— 2	18	Good improvement on both medications
	1.5	..	0.4	7.2	235	— 6	3	.....
22	2.8	..	0.1	4.7	360	—20	21	Much improved; dosage kept low because of cardiac status

many outpatient visits for basal metabolism, serum protein bound iodine, serum cholesterol, cardiac condition, and clinical status. These observations now extend, in uptake. Failure of this treatment to cause an increased uptake indicated athyreosis, while the hypothyroid patient with subnormal uptake in whom a significant in-

crease developed was classified as hypopituitary. The effect of thyroxin on the electrocardiogram was studied in a few cases. The effect of thyroxin on ovarian function in secondary hypothyroidism was emphasized.

CLINICAL MATERIAL

Ten patients discovered to have spontaneous athyreotic myxedema, which was demonstrated by a lack of response to thyrotropic hormone, were given sodium *l*-thyroxin by mouth with the results shown in table 1. Hypercholesterolemia was corrected and the patients have been well maintained in euthyroid condition for many months.

The usual starting dose was 0.1 mg. Extreme variability of maintenance dose is shown, one case requiring only 0.1 mg., one 0.2, one 0.3, one 0.6, and three 0.8 mg. It is to be noted that in one case (case 5), a 0.4 mg. daily dose produced hyperthyroidism, angina, and hyperiodemia.

The basal metabolic rate and serum protein bound iodine values of the patient in case 7 are shown in figure 1. Note that there is a lack of significant increase of radioactive iodine uptake after three injections of 15 mg. of thyrotropic hormone intramuscularly daily. No increase in protein bound iodine occurred as a result of the thyrotropic hormone treatment, and there was no variation in the basal metabolic rate. This conclusively demonstrates athyreosis. The early variations in the basal metabolic rate and protein bound iodine, as adjustment to the euthyroid status is gradually obtained, are most interesting.

A group of thirteen patients with severe hypothyroidism resulting from the eradication of hyperthyroidism by various means was treated with sodium *l*-thyroxin (table 2). These patients have been maintained in euthyroid condition for long periods of time. The maintenance daily oral dose was found to be from 0.4 mg. to 0.8 mg. Note that one patient (case 17), on 0.6 mg. of sodium

TABLE 3.—*Effect of Sodium l-Thyroxin Given Orally on Hypopituitary Hypothyroidism (Secondary)*

Case	Average Protein Bound Iodine Before Treatment, Mcg./100 Cc.	Medicament		Laboratory Tests While Patient Received Maintenance Dose of Medicament (Average)			Total Time of Treatment, Months	Clinical Condition
		Thyroid, Grains	Thyroxin, Mg.	Protein Bound Iodine, Mcg./100 Cc.	Cholesterol, Mg./100 Cc.	Basal Metabolic Rate, %		
23	3.0	1	...	4.2	272	−26	6½	Minimal improvement
	3.0	..	0.2	5.0	...	− 7	..	Some improvement; still has vertigo
	3.0	..	0.8	cholecystogram	...	− 3	18	Good improvement, but not yet euthyroid
24	1.9	..	0.6	6.7	228	0	23	Good
25	2.0	..	0.4	13.3	...	−11	14	Normal pregnancy and delivery at term. Spontaneous abortion at 3 mo. previous to treatment
26	3.3	..	0.4	7.0	162	− 4	18	No improvement clinically
27	2.6	..	0.8	7.5	...	+11	22	Menorrhagia improved; married
28	3.8 on 1 grain thyroid	..	0.8	4.7	204	− 5	16	Improved, married, working full time
29	3.0	..	0.8	10.3	...	− 1	..	Clinically toxic
	on 2 grains thyroid	..	0.4	5.3	...	−22	8	Much improved, not toxic
30	3.1	2	...	5.4	232	−29	4	Questionable improvement
	3.1	..	0.4	7.2	231	+ 4	30	Much improved
31	2.6	..	0.4	5.8	249	+ 7	8	On dosage for intermittent 3 week periods. Menorrhagia improved each time, but no improvement after medication discontinued

TABLE 4.—*Clinical Comparison of Desiccated Thyroid and Sodium l-Thyroxin Given Orally**

Case		Desiccated Thyroid U.S.P., Grains per Day			Sodium *l*-Thyroxin, Mg. per Day				
A	Dosage	3.0	5.0	...	0.4	0.6	1.0	...	...
	Protein bound iodine	4.0	5.0	...	3.1	8.0	10.6	...	...
	Clinical condition †	2+	1+	...	2+	3+	1+	...	...
B	Dosage	2.0	...	...	0.4	0.8	1.0	...	...
	Protein bound iodine	2.4	...	...	7.4	5.7	8.6	...	...
	Clinical condition	3+	...	...	1+	1+	1+	...	...
C	Dosage	5.0	...	...	0.4	0.6	0.8	...	...
	Protein bound iodine	2.5	...	...	6.4	10.2	6.7	...	...
	Clinical condition	4+	...	...	3+	2+	1+	...	...
D	Dosage	2.0	3.0	5.0	0.3	0.6	0.8	1.0	None
	Protein bound iodine	3.1	4.0	4.0	5.0	6.7	4.8	10.2	2.2
	Clinical conditions	2+	2+	2+	2+	0	2+	1+	2+
E	Dosage	5.0	...	...	0.4	0.8	0.8	...	...
	Protein bound iodine	2.0	...	...	6.9	11.9	9.5	...	...
	Clinical condition	4+	...	...	2+	1+	1+	...	...
F	Dosage	1.0	3.0	5.0	0.3	0.3	0.6	0.8	...
	Protein bound iodine	4.0	3.2	5.4	4.4	6.4	6.3	5.3	...
	Clinical condition	2+	2+	2+	2+	1+	1+	1+	...

* The data are presented from the practice of Dr. R. R. Commons.
† Estimated degree of hypothyroid clinical state: Myxedema = 4+, Euthyroidism = 0.

l-thyroxin for two years, became thyrotoxic with hyperiodemia during the last month of this period and was later well adjusted on 0.3 mg. daily.

Ten patients affected by secondary or hypopituitary hypothyroidism (table 3) indicated by positive response to thyrotropic hormone have been maintained on dosage

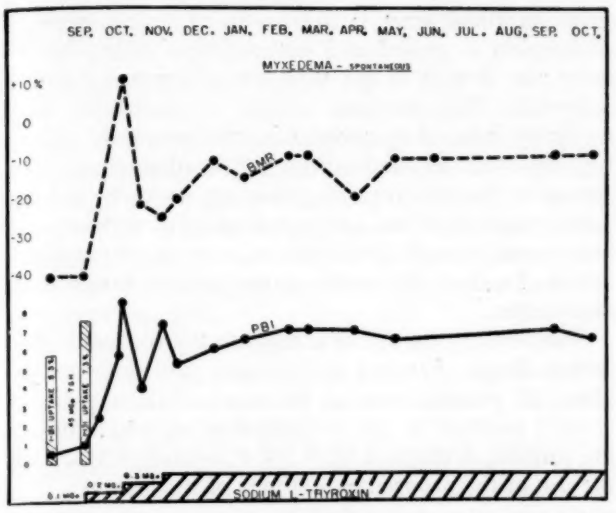

Fig.1.—Basal metabolic rate (BMR) and serum protein bound iodine (PBI) in a case of spontaneous myxedema (case 7). Thyroid-stimulating hormone (TSH) was given at the beginning of the period.

of 0.2 mg. to 0.8 mg. of sodium *l*-thyroxin. Note that in case 23, 0.2 mg. of thyroxin produced about the same effect as one grain of U. S. P. desiccated thyroid, but four times that amount, i. e., 0.8 mg. daily, led to a loss of 30 lb. (13.6 kg.) of overweight, with a high protein bound iodine.

In general it may be concluded that with proper adjustment of dosage for the individual patient, sodium *l*-thyroxin given orally maintained these patients in euthyroid status for a long period of time, in some instances for more than two years.

THYROID DOSAGE IN HYPOTHYROIDISM

It is our contention that a large number of hypothyroid patients are usually undertreated. In a special study, 14 patients with myxedema were recalled to estimate the adequacy of therapy. These patients had been put on the usual dosage of desiccated thyroid by competent members of the hospital staff. In 9 of the 14 patients the protein bound iodine value was found to be grossly subnormal, and in only two cases was it completely normal (fig. 2). In the present study of thyroxin our intention was to determine the highest tolerable dose; not infrequently an excessive dose was given, which after several months caused hyperiodemia and thyrotoxicosis. Reduction of dosage was followed by normal values and euthyroidism. Thus a dose that is well tolerated for some time with high or even supernormal serum protein bound iodine values may on occasion rapidly induce hyperthyroidism. The converse of this has already been reported,[6] i. e., a dose of desiccated thyroid that seems adequate may, after several months, be accompanied by a falling away of the serum protein bound iodine value with double, triple, or quadruple amounts of the original dose required for the return of clinical euthyroidism.

Although it is not desirable to induce hyperthyroidism, this condition usually becomes clinically evident and is corrected; the subsidence into hypothyroidism, however, is not disturbing, and it remains unrecognized and uncorrected.

EQUIVALENCE OF THYROXIN AND DESICCATED THYROID

The attempt to establish the exact clinical equivalence of sodium *l*-thyroxin to desiccated thyroid, U. S. P., is difficult in practice. A patient in apparently satisfactory clinical condition who has been given desiccated thyroid is studied more carefully when placed on the new medication. We have the clinical impression of greater benefit from sodium *l*-thyroxin than desiccated thyroid in several cases. To judge by the serum protein bound iodine values in the same patient on the two drugs, (table 4) no strict interpretation of equivalence is possible. One tenth of a milligram of sodium *l*-thyroxin seems to have the clinical effect of one-half a grain of desiccated thyroid in some patients and to have the effect of one grain of that material in others.

It must be concluded that the dose of sodium *l*-thyroxin required for the production of the ideal clinical result must be found in the individual case by the determination of systemic conditions, the serum protein bound

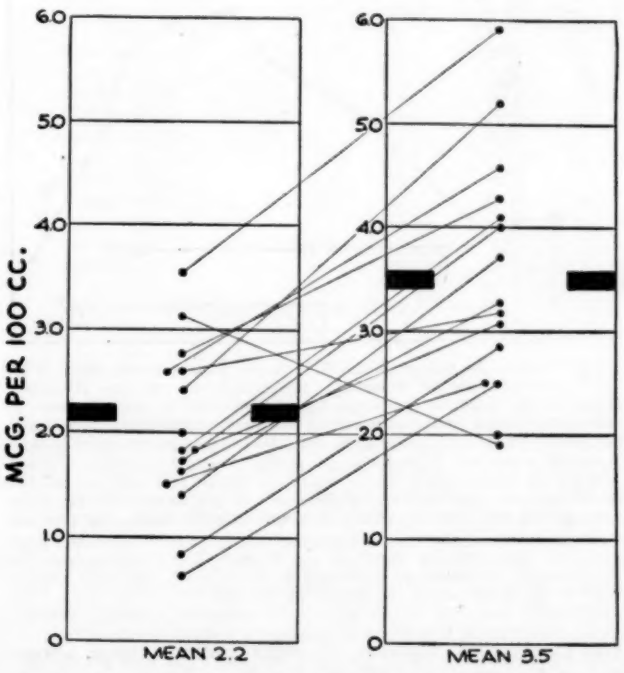

Fig. 2.—Serum protein bound iodine values of 14 patients with myxedema before and several months after prescription of desiccated thyroid.

iodine, the basal metabolic rate, and the efficiency of the patient. Furthermore, the dosage requirement must be revised in each new case at intervals of a few months. It is our practice to give 0.05 mg. daily by mouth, as the initial dose, with progressive increases to the level that gives the best results; this may vary from 0.2 mg. to 1.0 mg.

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EFFECTS OF THYROXIN

Effect on the Myocardium.—The electrocardiogram during the early days of treatment of hypothyroidism with thyroxin indicates that changes in the myocardium begin before the accumulation of thyroid hormone in the blood has reached normal concentration and before the basal metabolism has reached the euthyroid level. In case 7, after only eight days of administration of 0.1 mg. of sodium *l*-thyroxin daily, the electrocardiogram already showed changes indicating recovery when the serum protein bound iodine level was only 2.3 mcg. After the patient had been treated for 8 days at the next level of medication, 0.2 mg., i. e., after 35 days of treatment altogether, the electrocardiogram appeared normal; but after three and one-quarter months on the third level of medication, 0.3 mg., with the serum protein bound iodine and the basal metabolic rate in the higher normal ranges, the electrocardiogram suggested overdosage, i. e., the potential was excessive and the T waves abnormally high

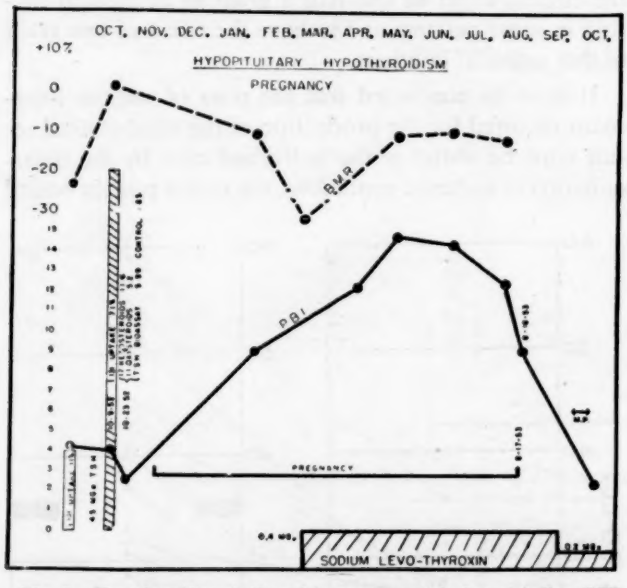


Fig. 3.—Hypothyroidism indicated by serum protein bound iodine (PBI) of 2 mcg. per 100 cc. (case 25). Miscarriage of previous pregnancy. Hypopituitary cause of hypothyroidism is indicated by great increase of radioactive iodine uptake after 15 mg. of thyroid-stimulating (thyrotropic) hormone (TSH) was given daily for three days. Adrenocorticotrophic hormone production is indicated by normal values for urinary steroids. Absence of thyrotropic hormone from the serum indicated by negative thyrotropic hormone bioassay. Maintenance of pregnancy with characteristic extreme elevation of serum protein bound iodine during last trimester is shown with sudden postpartum fall in serum protein bound iodine. Basal metabolic rate (BMR) is shown at top of chart. The 17-ketosteroids and 11-oxysteroids are measured in milligrams per 24 hours. The TSH bioassay result is the mean acinar cell height, in microns.

and peaked. A number of other patients have shown the early restorative effect of sodium *l*-thyroxin on the myocardium.

Effect on Pituitary Function.—Among the 10 patients (table 3) with secondary or hypopituitary hypothyroidism, various ovarian functional disorders were frequent. These were amenorrhea, menorrhagia, miscarriage, oligomenorrhea, and metrorrhagia. Usually, with the administration orally of sodium *l*-thyroxin in the daily dosage shown, these menstrual disorders were corrected, and, in one patient who had previously miscarried, normal successful termination of a pregnancy occurred; a serum protein bound iodine of 14 mcg. per 100 cc., characteristic of normal pregnancy, was recorded during treatment with only 0.4 mg. of sodium *l*-thyroxin daily (fig. 3). True physiological improvement of pituitary ovarian interrelation was thus promoted by this thyroid medication.

SUMMARY

The earlier clinical opinion that economically small doses of thyroxin were not regularly absorbed from the gastrointestinal tract is demonstrated to be incorrect. Myxedema is erased and euthyroidism maintained by daily oral dosage of less than one milligram of sodium *l*-thyroxin. Thyrotoxicosis caused by medication could easily be induced by overdosage and promptly relieved by reduction of medication. Myocardial changes, as shown by the electrocardiogram, are an early and sensitive indicator of the restorative effect of thyroxin. Improvement in ovarian function indicates the physiological action of sodium *l*-thyroxin on the pituitary-target organ mechanism.

Sodium *l*-thyroxin is an acceptable thyroid medication, with uniform chemical composition and biological potency. Its establishment as the standard thyroid drug in general practice, at an economical price, would obviate the variable strength of the U. S. P. animal products and the use of the proprietary extracts of the gland.

Food Potentials in the Sea.—Since more than 71% of the earth's surface is water covered, and an acre of sea is estimated to produce nearly three times as much as an acre of land, these relatively untapped food reserves deserve careful research to determine the best means for their utilization. It has been estimated that the total photosynthetic activity of the sea is approximately ten times that of all wild and cultivated plants on land. Some 13.5×10^{10} tons of carbon are believed to be fixed per year as a result of marine photosynthesis. In addition, marine harvests require no labor or expense for tilling, irrigation, or fertilization. They are produced in a complete nutrient solution which contains not only all the essential mineral elements leached from the land masses through the centuries, but also large quantities of dissolved gases—the oceanic content of carbon dioxide has been estimated at a million times that of the earth's atmosphere. Despite these facts, this vast harvest of oceanic food has received little research to evaluate its potential role in world feeding.

Some of the other products of the sea than fish and shellfish have been used as foods or to increase the production of land crops. Chief among these are the large seaweeds belonging to the brown, green and red algae, with their great capacity to accumulate important nutrients, which have found wide use as fertilizers and soil-conditioners. Due to their high mineral content, they have been used from very early times as manure to replenish the depleted coastal soils. . . . The use of seaweed as an animal food is a very old practice. Although it cannot be considered a complete animal food it is an excellent supplementary food and is now produced as such on the Pacific Coast. The Chinese and Japanese eat seaweed, thereby obtaining a fine source of minerals, vitamin A, and ascorbic acid. The water-soluble polysaccharides of the larger brown algae are used increasingly as stabilizers in food industries. Algin, for instance, has been used to replace gelatin as a stabilizer in ice cream and chocolate milk. The natives on some Pacific islands successfully use the fronds of large seaweeds to protect their freshly caught fish from rapid decomposition. The recent discovery of the antibiotic action of algal tissues explains this protection. The living algae contain powerful antibiotic substances to protect them from the myriad of bacteria constantly attacking them. Further research is needed to determine if the presence of the antibiotic substances in seaweeds, rather than their high mineral content, makes them such valuable supplementary foods for cattle.—Food Potentials in the Sea, *Nutrition Reviews*, March, 1954.

CLINICAL NOTES

APLASTIC ANEMIA FOLLOWING EXPOSURE TO CARBON TETRACHLORIDE

Bernard Straus, M.D., New York

The toxic effects of carbon tetrachloride on the liver and kidneys are well known, but a review of the literature reveals no information concerning the effect of this toxic agent on the bone marrow. Observations of three cases of aplastic anemia occurring after chronic exposure to carbon tetrachloride are therefore reported to supply this important material.

REPORT OF CASES

CASE 1.—A 28-year-old white man was admitted on Dec. 21, 1948, complaining of anorexia, epigastric distress, dark urine, and yellow discoloration of the skin of three weeks' duration. For the past six and one-half months, his work had frequently entailed the use, for two to eight hours a week, of sponges soaked in carbon tetrachloride in a small room ventilated only by a door. The patient was well developed, well nourished, and deeply jaundiced. The fundi were normal and the scleras were icteric. The heart and lungs were normal. The blood pressure was 100/77 mm. Hg, and the pulse rate was 80 per minute. The liver was enlarged one fingerbreadth below the costal margin and was nontender. The tip of the spleen was palpable.

Laboratory Findings.—On admission the hemoglobin level was 16.6 gm. per 100 cc. (photoelectric colorimeter), erythrocytes 4,700,000 per cubic millimeter, and leukocytes 5,600 per cubic millimeter, with 64% neutrophils, 28% lymphocytes, and 8% monocytes. Urinalysis revealed specific gravity 1.020, bile present, and albumin and glucose absent; the findings on microscopic examination were normal. The VDRL (Venereal Disease Research Laboratory) test for syphilis was negative. The cephalin flocculation was 2+, the icterus index was 162 units, the serum alkaline phosphatase level was 2.7 Shinowara units, and the thymol turbidity was 5 units per 100 cc. On Jan. 28, 1949, the serum bilirubin was 31 mg. per 100 cc. and the total serum protein was 6.6 gm. per 100 cc., with albumin 4.6 gm. and globulin 2 gm. per 100 cc. The prothrombin time was normal. One month later, the hemoglobin level had dropped to 8.6 gm. per 100 cc.; the red blood cell count was 2,500,000 per cubic millimeter; the white cell count was 3,500, with 52% neutrophils, 37% lymphocytes, 7% monocytes, and 4% eosinophils; and the platelet count was 90,000. Bleeding time was 70 seconds, and coagulation time was 5 minutes. A fragility test showed hemolysis beginning in 0.4% sodium chloride solution, and complete in 0.3% solution. There was 80% clot retraction in 24 hours. Serum bilirubin was 1.6 mg. per 100 cc., with van den Bergh direct 0.9 mg., indirect 0.7 mg. A sulfobromophthalein test on March 13, 1949, disclosed retention of 8% of the dye. Thereafter the patient received numerous blood transfusions. The erythrocyte and hemoglobin values varied with the transfusions, falling to about 2 million per cubic millimeter when transfusion was omitted and rising as high as 5,400,000 per cubic millimeter with repeated transfusions. The white blood cell count stabilized at about 2,000 per cubic millimeter, with a differential of between 10 to 20% polymorphonuclear leukocytes, 70% lymphocytes, and 3 to 4% monocytes. Platelets were frequently not seen at all, and the highest count was 16,000 per cubic millimeter. The sulfobromophthalein test showed 7% retention on May 2, 1949; prothrombin time was normal at that time. A phenolsulfonphthalein test on July 8, 1949, was normal; cephalin flocculation was 2+, thymol turbidity was 1.4 units per 100 cc., serum bilirubin was 0.5 mg. per 100 cc., and the alkaline phosphatase level was 4.3 units per 100 cc. Coagulation time on July 12, 1949, was 23 minutes; the prothrombin time was normal. The results of sternal marrow examinations are shown in the table. Radiographic examinations of the chest and bones were normal.

Course.—The liver disease caused the predominant symptoms for three months, but during the third month anemia, thrombocytopenia, and leukopenia developed and progressed in severity, while the hepatic disease subsided except for mild residual damage as indicated by a 2+ cephalin flocculation test. There was persistent bleeding of the gums and one episode of hematuria. The patient was given many transfusions and received a total of about 500 cc. of blood per week. On Dec. 9, 1949, he suffered a severe gastrointestinal hemorrhage and despite transfusions died two days later. The clinical opinion was that the toxic hepatitis and the aplastic anemia were secondary to carbon tetrachloride poisoning.

Autopsy Findings.—The clinical diagnosis of aplastic anemia was confirmed. There were hemorrhages in the brain and intestinal tract, marked hemosiderosis, bacterial emboli in the blood vessels of all the viscera, and acute suppurative meningitis; there were also periportal fibrosis and fatty infiltration of the liver, which were considered to be the residuals of the toxic hepatitis.

CASE 2.—A 26-year-old man was admitted on March 16, 1949, complaining chiefly of anemia of 15 months' duration. He had been well until April, 1946, when he had a short episode of faintness and a sense of coldness. Similar episodes occurred during the next several months. In November, 1947, the patient noted that he was getting many more black and blue marks after playing football than was usual for him. From November, 1947, to May, 1948, he became increasingly fatigued and suffered many nose bleeds. In June, 1948, the red blood cell count was 1,900,000 per cubic millimeter and the hemoglobin level was 35% of normal. The patient was hospitalized elsewhere and given four blood transfusions and liver injections. Several months later he consulted a hematologist and was hospitalized at the Bayonne Hospital, where he received a transfusion and his spleen was removed on Sept. 9, 1948, after a diagnosis of thrombocytopenic purpura had been made. The patient had a stormy postoperative course requiring many blood transfusions during which he was transferred to the Bronx Veterans Hospital. The bruising tendency decreased, but the patient had continuous bleeding from the nose and gums. The history revealed that the patient's chief occupation throughout almost three years of military service, ending Oct. 18, 1945, had been cleaning gun parts with kerosene and carbon tetrachloride in a small shack with very poor ventilation. He was exposed to fumes and had direct physical contact with the cleaning fluid. Of his 10 fellow workers, jaundice had developed in at least one.

Percentage of Various Elements in Bone Marrow of Patient in Case 1

Type of Cell	March 25, 1949 *	May 10, 1949 †	Sept. 6, 1949 ‡
Reticulum cells	0	0	0
Myeloblasts	1	2	0
Promyelocytes	0	0	0
Myelocytes	15	1	4
Metamyelocytes	0	0	3
Stab	20	17	14
Segmented	15	12	10
Lymphocytes	27	31	52
Eosinophils	1	0	0
Plasmacytes	1	0	0
Erythroblasts	0	0	2
Normoblasts	20	36	12
Total count per cubic millimeter	22,000	8,000	...

* Hypoplastic marrow.
† Hypoplastic, relative lymphocytosis.
‡ Markedly aplastic.

The patient was a well-nourished, well-developed young white man in no distress. The mouth revealed a few petechial hemorrhages on the buccal mucosa and soft palate. The lungs were normal. The heart was not enlarged and had a regular rhythm. The blood pressure was 126/70 mm. Hg. The pulse

From the Medical Service, Veterans Administration Hospital, Bronx, N. Y.

rate was 82 per minute. There was a large healed postoperative scar on the abdomen (splenectomy). No masses or viscera were palpated. A few petechial hemorrhages were present in the skin.

Laboratory Findings.—The red blood cell count was 2,500,000 per cubic millimeter, hemoglobin level 8.8 gm. per 100 cc., the white blood cell count 3,300, with 10% polymorphonuclear leukocytes, 83% lymphocytes, and 7% monocytes, and the platelet count 30,000. The sedimentation rate was 23 mm. per hour. The serologic test for syphilis was negative; serum bilirubin 2.5 mg. per 100 cc., cephalin flocculation 1+, prothrombin time normal, and urinary urobilinogen positive in 1:10 dilution. Clot retraction began in 31 minutes, but there was very poor retraction in 8 hours. A fragility test was normal. The bleeding time was 2 minutes, and the coagulation time was 5 minutes. The Rumpel-Leede phenomenon was strongly exhibited. Total serum protein was 7 gm. per 100 cc., with albumin 4.9 gm. and globulin 2.1 gm. Sternal marrow examination on April 8, 1949, disclosed hypoplasia with a relative lymphocytosis and plasmacytosis. Another sternal marrow examination on Sept. 2, 1949, revealed a similar condition with 1% reticulum cells, 0.5% myeloblasts, 3.5% myelocytes, 1.5% metamyelocytes, 1% juvenile forms, 19.5% plasma cells, 69% lymphocytes, and 5% normoblasts. There were no segmented forms, no megakaryocytes, and no erythroblasts. The erythrocyte-leukocyte ratio was 20:1. Radiographic examinations of the chest and bones were normal.

Course.—For the first six months of hospitalization the patient's condition was fairly good. He was given 500 or 1,000 cc. of blood each week. After many blood transfusions, two large, deeply pigmented areas developed bilaterally in the skin of the medial surface of the arms. A biopsy was done on skin from the right arm, and hemosiderosis was found. By October, 1949, the patient had received over 100 transfusions, of which 30 were given in this hospital. On Nov. 14, 1949, he had a severe gastrointestinal hemorrhage and was treated with transfusions and daily administration of 300 mg. of toluidine blue by infusion. No effect resulting from the administration of toluidine blue was noted. In the third week of November, 1949, hematuria developed and, together with gastrointestinal bleeding, continued until death occurred on Dec. 11, 1949. The clinical diagnosis was aplastic anemia probably secondary to carbon tetrachloride poisoning.

Autopsy Findings.—Autopsy performed 16 hours after death disclosed large amounts of blood in the gastrointestinal tract, renal calices, and pelves. There was hemosiderosis of the liver, kidney, thyroid gland, and prostate. Slight periportal fibrosis was present. There was marked reduction of cellularity of the marrow. Autopsy diagnoses were aplastic anemia due to hypoplasia of bone marrow, and hemosiderosis.

CASE 3.—A 24-year-old white Italian auto mechanic was admitted on March 3, 1953, complaining of a rash of three weeks' duration. He had been in excellent health until three weeks prior to admission, when he noted the presence of a macular hemorrhagic rash over the lower extremities. Two weeks prior to admission he noted similar lesions on the arms and forearms and, one week later, on the chest and shoulders. The lesions were well circumscribed and were about 2 mm. in diameter. There was no pruritus. About 10 days before admission the patient consulted a physician because of the rash, and a blood cell count was done that revealed depression of platelets. For two days before admission the patient had bleeding from the gums, and on the day of admission one episode of epistaxis lasting for two hours occurred. The patient also noted weakness, dizziness, and a loss in sense of well-being for several days before admission. He had worked in a garage for the first two months of 1953; during this period, he cleaned his tools with carbon tetrachloride. He also used this solvent to clean car upholstery once or twice a week. The exact period of time that he was exposed to this agent was not determined. The patient had been treated for malaria with chloroquine while in Korea in June, 1952, and had been given some medication, possibly primaquine, in December, 1952.

The patient was well developed and well nourished. There were scattered purpuric lesions on the skin 2 mm. in diameter; most were confined to the lower extremities, but similar lesions were also present on the arms, chest, back, neck, and shoulders. There was crusted blood in the nostrils and active bleeding from the gums. The remainder of the examination was within normal limits. The liver and spleen were not palpable. The blood pressure was 100/60 mm. Hg.

Laboratory Findings.—The urine was normal. A VDRL test for syphilis was negative. The hemoglobin level was 9.9 gm. per 100 cc., the red blood cell count 3,100,000 per cubic millimeter, and the white blood cell count 4,650, with 40% neutrophils, 5% juvenile forms, 54% lymphocytes, and 1% monocytes. The Rumpel-Leede phenomenon was exhibited. Bleeding time was 15 minutes; clotting time was 5½ minutes. There was poor clot retraction in 24 hours. The platelet count was 15,000 per cubic millimeter. The blood urea nitrogen was 19 mg. per 100 cc. and the total serum protein, 6.8 gm. per 100 cc.: albumin 4.7 gm., globulin 2.1 gm. The serum bilirubin was 1 mg. per 100 cc., van den Bergh direct 0.1 mg., indirect 0.9 mg. The cephalin flocculation was 1+; thymol turbidity 4.3 units per 100 cc., and prothrombin time 16.8 seconds, with a control of 14.7 seconds. The bone marrow was hypocellular with absence of megakaryocytes and diminution of platelets; the differential count was 0.5% myeloblasts, 8% myelocytes, 13% metamyelocytes, 22% band forms, 17% segmented forms, 34% lymphocytes, 0.5% monocytes, 1.5% eosinophils, 1.5% reticuloendothelial cells, 2% plasma cells, 0.5% erythroblasts, and 3.5% normoblasts. No tumor cells were seen.

Course.—The patient was given strict bed rest and supportive transfusions. Successive marrow aspirations revealed persistent hypocellularity. On completion of all laboratory studies, the patient was given 100 mg. of cortisone daily. There was an improvement in the purpuric eruption; nevertheless, the Rumpel-Leede phenomenon persisted. Bleeding from the gums and minor episodes of epistaxis continued, and blood cell counts showed a persistent mild anemia, slight leukopenia with normal differential counts, and marked thrombocytopenia, with the platelet count ranging from 5,000 to 10,000 per cubic millimeter. On the 18th hospital day the patient had severe bleeding from the gums and nose. One liter of fresh blood was given, and the bleeding stopped. On the 25th hospital day there was a severe epistaxis requiring packings and transfusion. Blood was also noted in the external auditory canals, and flecks of blood on both tympanic membranes. The temperature rose to 103 F. Cortisone administration was gradually discontinued, and streptomycin and penicillin were given. The patient had daily temperature elevations to 105 F and 106 F, and his condition rapidly became worse, though bleeding had almost ceased. Although the hemoglobin level was 13 gm. per 100 cc. and the red blood cell count was 4 million per cubic millimeter, the white cell count fell precipitously, and on the 30th hospital day was 550 with 100% lymphocytes. The patient lapsed into coma and died on the 36th day of hospitalization.

Autopsy Findings.—There was massive hemorrhage into the gastrointestinal tract and lesser hemorrhages in the pleural spaces, the diaphragm, and the myocardium. The bone marrow was markedly hypoplastic, and large areas were replaced by fat. There were some immature erythrocytes and lymphocytes, but no granulocytes or megakaryocytes were present.

This patient received chloroquine and possibly primaquine for malaria in 1952. Unlike quinacrine (Atabrine), neither of these two antimalarial drugs is known to injure bone marrow.

COMMENT

Many chemical and physical agents have produced aplastic anemia. These include benzol, organic arsenicals, gold compounds, nitrogen mustards, bismuth, mercury, colloidal silver, dinitrophenol, trinitrotoluene, hair dyes, sulfonamides, radioactive substances, certain anticonvulsives and antihistamines, chloramphenicol, thiosemicarbazone, streptomycin, thiouracil, aminopyrine, and quinacrine. A significant number of cases of aplastic anemia occur for which no cause has been determined. It seems possible that some of these cases are due to chemical toxins that have not hitherto been associated with the disorder. Carbon tetrachloride, like benzol, is

a widely used industrial solvent. Unlike benzol, it does not contain a benzene ring, the chemical formula being CCl_4; but in view of the varying structure of compounds implicated in the production of refractory anemia, its molecular structure is not evidence against possible bone marrow toxicity.

The mechanism producing the hemorrhagic phenomena that have been observed following exposure to carbon tetrachloride is not clear. Possibly the bleeding tendency is due to prolongation of the prothrombin time as a consequence of hepatic injury. Such effects have been observed experimentally. The subconjunctival hemorrhages that occur have been ascribed to severe coughing due to pulmonary irritation induced by the agent. The vapors of carbon tetrachloride may also have a direct irritant action on the conjunctivas and mucous membranes. Finally, a direct toxic effect on the bone marrow must be considered; it is suggested that the cases reported here are examples of this effect. Most cases of carbon tetrachloride poisoning that have been described have resulted from acute exposure. In these cases, the immediate effects may resemble those of an anesthetic such as chloroform; the delayed effects are injury to the kidney and liver. In acute cases, there is an increased tendency to hemorrhage. The effects of chronic poisoning have been reported in relatively few cases. Since carbon tetrachloride has a cumulative action with repeated exposures, bone marrow depression may become manifest only after a long series of minor insults by this toxin. It is significant that, in the three cases reported, exposure to carbon tetrachloride was of a chronic nature, exposure having continued for six and one-half months, almost three years, and two months, respectively. The bone marrow injury may be associated with manifest hepatic damage as in case 1 or may occur alone as in cases 2 and 3.

The observations reported here and the widespread use of carbon tetrachloride under hazardous conditions, such as poorly ventilated quarters, suggest that all patients with aplastic anemia should be closely questioned about a history of exposure to carbon tetrachloride. The importance of avoiding exposure is obvious.

SUMMARY

Three patients with aplastic anemia following chronic exposure to carbon tetrachloride died. In one case, overt injury to the liver was also sustained. It is suggested that chronic exposure to this widely used industrial solvent may result in irreversible bone marrow damage. Carbon tetrachloride poisoning should be considered as a possible etiological factor in cases of aplastic or refractory anemia.

123 E. 83rd St. (28).

Mortality in Early Infancy.—The annual loss of life in early infancy is still very high in the United States. More than 76,000 babies a year die within one month of birth; this is approximately as many deaths as occur annually in the broad age range from one month up to 20 years. Mortality is especially high soon after birth. Of all the deaths in the first four weeks, about half take place on the very day of birth; nearly seven eighths occur within the first week.—Conserving the Life of the Newborn, *Statistical Bulletin Metropolitan Life Insurance Company*, November, 1953.

SEVERE DRUG SENSITIVITY REACTION TO PHENINDIONE (PHENYLINDANDIONE)

Norman Makous, M.D.
and
Joseph B. Vander Veer, M.D., Philadelphia, Pa.

In 1947, Soulier and Gueguen [1] first reported the clinical use of phenindione (phenylindandione or Danilone) as an anticoagulant. Blaustein and others [2] have had the widest reported experience with this drug. Except for the expected complication of minor bleeding, reports of untoward reactions have not appeared in the literature since the original paper was published in 1947. In our limited experience with 47 patients, there have been two cases of hematuria necessitating discontinuance of this anticoagulant and in a third case a severe toxic reaction due to phenindione sensitivity. The report of the latter case follows:

REPORT OF A CASE

A 42-year-old Negro woman was admitted to the Pennsylvania Hospital on May 8, 1953, with thrombophlebitis of the left leg. For one month swelling, stiffness, and popliteal tenderness had been present. The patient gave a history of menorrhagia and left lower abdominal discomfort for one year and had been seen several times during the preceding two months as an outpatient in the gynecology department. Analgesics were necessary daily for pain relief. Six years previously she had been told she had a "fibroid tumor." The family history, the patient's history, and the systemic review were otherwise noncontributory.

Physical examination showed an overweight woman with pitting edema 3+ from the left foot to midthigh. The left ankle was red and was warmer than the right one, and there was tenderness on deep palpation in the upper calf and left popliteal area. Homan's sign was elicited on the left leg. Left lower abdominal tenderness was present on deep palpation. Pelvic examination showed that the uterus was about four times normal size. The blood pressure in the arms was 145/90 mm. Hg bilaterally. The hemoglobin level was 12.4 gm. per 100 cc. eight days prior to admission (Sheard-Sanford photoelectric method). The red blood cell count was 4,300,000, and the white blood cell count was 7,300 per cubic millimeter. The urinalysis showed no abnormal results. The specific gravity of the urine was 1.022. Serologic tests for syphilis were nonreactive. Chest roentgenograms on the 6th and 15th hospital days were normal.

Hospital Course.—Procaine penicillin G, 300,000 units in aqueous suspension, was administered intramuscularly on the first hospital day and daily thereafter for 11 days. Administration of phenindione, 3.725 gm. total dosage in 14 days (about 125 mg. given twice daily), was started at the same time. The prothrombin time (Quick's one stage method with 12-second control) ranged between 9% and 23% from the 5th to the 15th day. On the fifth day, a nonproductive cough appeared that persisted for one month. The signs of thrombophlebitis subsided completely by the seventh day. Slight vaginal bleeding began on the 11th day. On the 16th day, about 10 hours after a prothrombin time of 19% (determined at 10 a. m.) and over 48 hours after the last dose of phenindione, the patient had a chill. This was followed by nausea and headache. The oral temperature was 101.6 F. After a step-like increase, the temperature

From the Cardiovascular Service of the Pennsylvania Hospital.
Dr. David S. Marshall II made the illustrations used in this report.

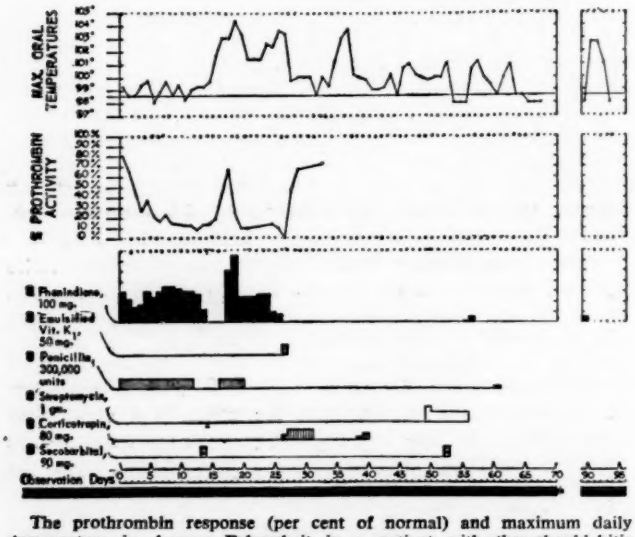
1. Soulier, J. P., and Gueguen, J.: Action hypoprothrombinémiante (anti-K) de la phényl-indane-dione étudiée expérimentalement chez le lapin: son application chez l'homme, Compt. rend. Soc. de biol. **141**: 1007 (Oct.) 1947.

2. Blaustein, A.; Shnayerson, N., and Wallach, R.: Clinical Use of a New Anticoagulant, Phenylindanedione. Report of 400 Cases, Am. J. Med. **14**: 704 (June) 1953.

reached a maximum of 104.6 F on the 19th day. Pain in the eyes was a prominent symptom, and vomiting accompanied the malaise.

On the 18th day, left popliteal tenderness reappeared. Anticoagulant therapy was instituted again with heparin sodium, 50 mg. administered intravenously every 4 to 6 hours and continued for 36 hours. Phenindione was also administered over a 10 day period beginning with 500 mg. on the first day and 650 mg. on the second day of therapy (2.75 gm. total dosage). The prothrombin concentration fell from 67% to 10% in two days and remained at 10% until the 10th day of therapy. The hemoglobin level was 12 gm. per 100 cc. with a red blood cell count of 4 million, a white blood cell count of 5,000 per cubic millimeter, and a normal differential count.

On the 19th day the white blood cell count was 3,100 per cubic millimeter with 80% neutrophils and the urinalysis showed normal results. The specific gravity of the urine was 1.002. The heterophil antibody titer was not significant. Blood cultures were negative on two successive days. A maculopapular rash developed at this time that involved the legs and arms to a lesser extent than it involved the trunk and face. Red and white punctate spots were seen on the palate but were not seen on the buccal mucosa. The conjunctivas were congested, and a minimal posterior cervical lymphadenopathy was present. A



The prothrombin response (per cent of normal) and maximum daily temperature in degrees Fahrenheit in a patient with thrombophlebitis treated with the anticoagulant phenindione (phenylindandione).

serosanguineous postnasal drip was present from the 20th to the 28th day. By the 27th day the patient's general condition had deteriorated. A pulse rate of 106 per minute, which was the maximum for the entire febrile course, accompanied the temperature of 103.4 F. The fading rash again flared and became pruritic. Dryness of the mouth, polydipsia, and polyuria were prominent symptoms. Slight bleeding from the nose and vagina continued, a hematoma developed at the site of a venipuncture, and the Rumpel-Leede phenomenon was elicited. The prothrombin concentration, in spite of reduction of the phenindione dosage the preceding 48 hours, fell to below 10%. The white blood cell count was 5,100 per cubic millimeter with 51% neutrophils, 1% metamyelocytes, 34% lymphocytes, 4% monocytes, 9% eosinophils, and 1% plasma cells. The blood urea nitrogen level was 9 mg. per 100 cc. The urine showed albumin (2+) and a positive culture of Bacillus proteus. The phenindione therapy was discontinued, and vitamin K_1 emulsion (50 mg.) was given intravenously; corticotropin in gelatin, 20 mg., was given every six hours for 18 doses. The prothrombin concentration was 48% the next day (28th hospital day), and nasal bleeding ceased. By the 30th hospital day, the rash had nearly cleared and the oral temperature was 100 F or less. Dryness of the mouth and frequent urination were still present. Jaundice became apparent for the first time, and the liver edge was palpable and tender. The white blood cell count was 22,500 per cubic millimeter with numerous blast cells and atypical lymphocytes. On the 33rd day the white blood cell count was 24,700 per cubic millimeter with 29% neutrophils, 1% metamyelocytes, 15% myelocytes, 27% blasts, 5% plasma cells, 22% eosinophils, and 1% monocytes; platelets were reduced on the blood smear. The total serum bilirubin was 14.0 mg. per 100 cc.; one minute direct bilirubin, 9.2 mg. per 100 cc.; alkaline phosphatase (modified Bodansky), 28.3 units; thymol turbidity, 15.5 units; cephalin flocculation, 3+; and total protein, 5.4 gm. per 100 cc. with albumin 3.1 gm. per 100 cc. The heterophil antibody titer remained insignificant on the 34th day, and the results of the electrocardiogram were normal except for a prolonged QT interval.

On the 35th day, the temperature rose above 100 F and continued to climb for three days. Corticotropin in gelatin, 75 mg., was given over a period of 12 hours. The white blood cell count was 12,300 per cubic millimeter with 52% neutrophils, 1% metamyelocytes, 37% lymphocytes, 1% monocytes, 1% eosinophils, 1% basophils, 2% plasma cells, and 5% blasts. No lupus erythematosus cells were found in the peripheral blood. The total serum bilirubin level fell to 8 mg. per 100 cc., but the thymol turbidity level rose to 33.4 units. By the 47th day, dryness of the skin and small scattered wheals were distressing because of pruritus. A skin, muscle, and lymph node biopsy showed only reactive hyperplasia of the lymph node. The hemoglobin level was 7.9 gm. per 100 cc. with 3,200,000 red blood cells and 10,200 white blood cells per cubic millimeter with a 10% eosinophil count. The liver function was improved. The patient received three 500 cc. blood transfusions.

On the 54th day, after nine days of streptomycin therapy, the genitourinary tract symptoms subsided. The patient became afebrile for three days. The liver was palpable 4 cm. below the right subcostal margin, and the jaundice had cleared. The patient was discharged at her insistence on the 62nd day.

Sensitivity Tests.—There was no family allergic history. The patient had no history of food or drug reaction, hay fever, asthma, urticaria, or previous dermatological afflictions. The patient had taken Anacin (a mixture of acetophenetidin, aspirin, and caffeine), two to three tablets per day, and aspirin, one to two tablets per week, during the preceding year. Ingestion of these during hospitalization caused no reaction. Secobarbital (Seconal), 90 mg., was taken on the 14th hospital day, and this dose was repeated on the 53rd day without reaction. Procaine penicillin G, 1,000 units in aqueous suspension, was given to the patient intradermally without local reaction. About 0.05 mg. of phenindione in 0.1 cc. of water was injected intradermally. A pseudopod appeared immediately at the injection site without local reaction other than slight erythema. Isotonic sodium chloride solution, 0.1 cc. given intradermally, produced a wheal larger than that produced by the drugs but without pseudopods or erythema.

On the evening of the 56th hospital day, after 72 hours of normal temperature, phenindione, 12.5 mg., was given to the patient. A dose of 50 mg. was given the next noon. A temperature that reached 101 F was accompanied by malaise, nausea, and pruritus; it persisted for four days. After 24 hours with no fever, the patient was given procaine penicillin in aqueous suspension, 25,000 units intramuscularly, without reaction or fever. The patient was discharged from the hospital the following day. A fever reaching a high of 101 F and unaccompanied by other symptoms was present for 36 hours after the patient arrived home.

After 20 days of an uneventful convalescence at home, the patient was seen as an outpatient. Physical examination showed no abnormalities except for dry skin and deep, painful skin fissures of the heels. The total serum bilirubin level was 1.5 mg. per 100 cc., sulfobromophthalein (Bromsulphalein) retention at 45 minutes 12%, and thymol turbidity 12.5 units. Phenindione, 50 mg., was given orally at this time. Within one hour the patient noticed a tingling of the skin and a chilly sensation. Malaise and nausea developed, followed by vomiting. The temperatures recorded by the patient were elevated for two days, and reached a high of 102 F. The symptoms subsided as the temperature dropped to normal. Several weeks after this episode, her skin symptoms became more severe. One week after

this provocative test the hemoglobin level fell to 8.6 gm. per 100 cc. with 2,200,000 red blood cells per cubic millimeter. It rose 1 gm. per 100 cc. over the next two weeks. The patient continued to improve after this exacerbation of her symptoms. The figure illustrates the prothrombin activity and febrile response in relation to the drugs administered.

COMMENT

Soulier and Gueguen reported as toxic reactions to phenindione dryness of the mouth, polydipsia, polyuria, tachycardia, and scarlatiniform rashes. They believed renal damage, manifested by hematuria and low specific gravity of the urine, was caused by tubular deposition of drug crystals. Blaustein has reported diarrhea as a side reaction. Associated ecchymosis, epistaxsis, hemoptysis, gastrointestinal bleeding, and hematuria have also been reported,[3] as well as gross bleeding into operative incisions.[4] We have noted petechiae involving the lower legs in one patient, as have Preston and others.[5]

In the present case tachycardia was not present. The rash was morbilliform instead of scarlatiniform. Although nosebleeds were frequent, they were not troublesome. Hematuria did not occur, but polyuria with low specific gravity of the urine was present. Renal damage was not presumed to be present on the basis of this finding alone, as a large oral intake of fluids secondary to the thirst might be responsible. The other complications were severe and were distinctly drug sensitivity reactions. The acute febrile episode began 15 days after the beginning of phenindione therapy and was accompanied by dermatitis, adenitis, leukemoid reaction, hepatitis, and anemia.

The skin test for reaction to phenindione was positive, though not strikingly so, and the test for reaction to penicillin was negative. Passive transfer skin tests were unsuccessful. The oral provocative tests with phenindione resulted in febrile and systemic response.[6] There was no such reaction to penicillin. The fever that developed about 24 hours after the penicillin injection seemed to be caused by the unaccustomed physical activity incident to the patient's returning home. The other drugs (aspirin, Anacin, and secobarbital), administered prior to the sensitivity reaction were given to the patient later during hospitalization without increased febrile response or symptoms.

The toxic reactions to phenindione noted by Soulier and Gueguen accompanied single doses in the range of 10 to 20 mg. per kilogram of body weight. Our patient received an average of 266 mg. (3.24 mg. per kilogram) daily the first 14 days. This maintenance dose is larger than that found necessary by Blaustein. The patient falls into the "resistant" group described by him. This resistance was relative and not absolute, for the patient had an adequate prothrombin time response and was readily maintained in the therapeutic range (see figure). It may be, however, that larger doses, though effective, will be related to an increased toxicity of the drug. Another factor in this case possibly responsible for the severity of the reaction may be that therapy was reinaugurated during the initial phase of the sensitivity reaction and that during the first 24 hours the patient received 1150 mg., or 14 mg. per kilogram of body weight, of phenindione. This falls within the toxic range noted by Soulier and Gueguen.

SUMMARY

In a patient with thrombophlebitis who was treated with the anticoagulant drug phenindione (phenylindandione), a severe general reaction appeared with hepatitis, jaundice, a leukemoid blood picture, skin rash, and anemia. Subsequent studies and observation suggest that an acquired sensitivity to this drug was the cause of the illness.

330 S. 9th St. (7) (Dr. Vander Veer).

3. Drinan, F. W.; Sise, H., and Moloney, W. C.: The Use of the Anticoagulant Phenylindanedione in Ambulatory Patients, Proc. New England Cardiovas. Soc. **11**: 9, 1952-1953.

4. Brown, K. W. G., and MacMillan, R. L.: The Anticoagulant Effect of Phenylindanedione in Thromboembolic Disorders, Am. J. M. Sc. **225**: 495 (May) 1953.

5. Preston, F. W.; O'Connor, W. R.; Thompson, C. E., and Christensen, E. N.: Clinical Use of the Anticoagulant Phenylindanedione: Report of 74 Cases, Circulation **6**: 515 (Oct.) 1952.

6. The provocative tests were done with two different commercial preparations of phenindione, Hedulon and Danilone.

USE OF PRESCALENE LYMPH NODE BIOPSY IN ABSENCE OF PALPABLE SUPRACLAVICULAR NODES

REPORT OF FORTY-ONE CASES

James H. Cuykendall, M.D., Denver

In 1949, Albert C. Daniels [1] described a method of biopsy that is useful in diagnosing intrathoracic diseases. The method consists of removal of the lymph-node-bearing adipose tissue overlying the supraclavicular portion of the scalenus anterior muscle. This tissue was found to be easily accessible with the patient under a local anesthetic. Daniels reported five cases in which palpable nodes were absent and the biopsy material was found to contain lymph nodes involved by disease processes of pulmonary origin. The disease process was Boeck's sarcoid in two cases, carcinoma in two cases, and silicosis in one case.

From August, 1949, to February, 1953, prescalene lymph node biopsy was done on 41 patients at the Veterans Administration Hospital, Fort Logan and Denver.[2] In these cases, a single density in the roentgenogram of the chest, an unresolving pneumonitis, or an unexplained hydrothorax was present. Bronchoscopic examination was made in every case. Bronchial washings, sputum, gastric washings, and pleural fluid were studied bacteriologically and cytologically. The usual review of systems was carried out in an attempt to exclude disease processes of extrathoracic origin. When the possibility of involvement of the lung by neoplasm or granuloma (tuberculous or tuberculoid) remained, prescalene lymph-node-bearing tissue was removed in the attempt to show metastasis or involvement by granuloma.

Resident in Radiology, Veterans Administration Hospital.

This paper was read at the Colorado Trudeau Society meeting, Denver, April 18, 1953.

The case material used in this study was obtained from Dr. William B. Dublin, Chief of Laboratory Service, and Dr. John R. Durrance, Chief of Chest Service.

1. Daniels, A. C.: A Method of Biopsy Useful in Diagnosing Certain Intrathoracic Diseases, Dis. Chest **16**: 360-367 (Sept.) 1949.

2. In August, 1951, the hospital was moved from Fort Logan to Denver.

OBSERVATIONS

The prescalene lymph nodes were involved by specific disease processes in eight cases. In three cases, metastatic carcinoma was present; in four cases, noncaseating tuberculoid granuloma (Boeck's sarcoid) was discovered; and in one case lymphosarcoma was found. In one of the cases of noncaseating tuberculoid granuloma, biopsy material taken from the other side after an interval of six months again showed the granuloma. In another of the cases of noncaseating tuberculoid granuloma, a biopsy in which an inadequate amount of material was obtained was followed, 10 days later, by an adequate biopsy.

In 33 cases, the prescalene lymph nodes showed no specific lesion at biopsy. In this group, diagnosis of intrathoracic neoplasm was effected by histopathological means in 15 cases. In 11 of these 15 cases bronchogenic carcinoma was found; in these 11 cases, diagnosis was established in 9 cases by thoracotomy, in 1 by autopsy, and in 1 by biopsy of a supraclavicular lymph node that was palpable later. Two malignant teratomas of the mediastinum were seen; diagnosis was made in one of these cases by thoracotomy, and in the other by biopsy of a supraclavicular lymph node that was palpable later. There were two cases of intrathoracic metastasis from carcinomas of extrathoracic origin. One of these cases was reported histologically as adenocarcinoma, which was probably of renal origin; the other was reported as malignant, epithelial, metastatic neoplasm of unknown site. The diagnosis was established by thoracotomy in one case and by biopsy of the chest wall in the other.

Among the cases of nonmalignant chest lesions were four of pneumonia and one each of abscess, bronchiectasis with pneumatocele, and tuberculosis. In these seven cases, diagnosis was made by histopathological methods (thoracotomy) in four cases and by bacteriological methods in three. In 11 cases, a definitive diagnosis of the disease condition was not established; bacteriological findings were not revealing and thoracotomy was not performed. In 7 of these 11 cases, the patients were discharged apparently free of disease. In these cases thoracotomy did not seem indicated and there was no positive bacteriological or other diagnostically significant finding. Of the remaining 4 of the 11 cases in which diagnoses were not established, the desired investigative procedures were refused by the patients in two cases and the patients died and permission for autopsy was not granted in two cases.

SUMMARY AND CONCLUSIONS

In 41 cases in which prescalene lymph node biopsy was performed there were 14 cases of bronchogenic carcinoma. In three of these, prescalene lymph node biopsy showed metastasis to the lymph nodes. There were two cases of intrathoracic malignant teratoma; these showed no metastasis. Prescalene lymph node biopsy in two cases of intrathoracic metastasis from carcinoma of extrathoracic origin similarly failed to show lymph node involvement. Four cases of noncaseating tuberculoid granuloma (Boeck's sarcoid) were seen; in all four cases, biopsy yielded positive results. In one of these cases, a second biopsy was necessary, since the tissue removed on the first occasion was considered inadequate. In one case of lymphosarcoma, biopsy yielded positive results. Biopsy of prescalene lymph nodes in cases in which palpable lymph nodes were absent has proved to be of some value in the diagnosis of intrathoracic diseases, especially granulomas (Boeck's sarcoid) and malignant neoplasms.

1055 Clermont St. (20).

USE OF CORTICOTROPIN THERAPY FOR IDIOPATHIC ACQUIRED HEMOLYTIC ANEMIA

REPORT OF A CASE

Leo M. Meyer, M.D.
and
Norton D. Ritz, M.D., Brooklyn, N. Y.

In the recent literature dealing with the treatment of acquired hemolytic anemia, the action of corticotropin and cortisone is inferred to be equally efficacious. In one of the cases reported by Dameshek and Rosenthal [1] the patient relapsed when 200 mg. of cortisone, daily, was substituted for corticotropin; resumption of corticotropin therapy was again followed by remission of symptoms. At a later date, the same patient was treated with cortisone with continued beneficial response. In the case of acquired hemolytic anemia reported by Meyers and coworkers [2] there appeared to be no appreciable difference between the effects of cortisone and corticotropin when a favorable outcome could be produced by either drug. The case of idiopathic acquired hemolytic anemia to be reported is interesting because adequate doses of cortisone failed to control the hemolytic process, whereas administration of corticotropin produced a sustained remission.

A white woman, age 43 years, was admitted to the Swedish Hospital on Jan. 14, 1953, with chief complaints of weakness, dyspnea, and palpitation that had lasted for three weeks. Shortly before onset of these symptoms she had received therapy with penicillin for an erysipeloid infection and phlebitis of the right leg. Except for moderate elevation of blood pressure the patient had always been in good health. The patient's mother had died of aplastic anemia; a brother died of Hodgkin's disease.

Temperature, pulse rate, and respirations were normal. Physical examination disclosed severe pallor, moderate obesity, slight jaundice of the scleras and skin, blood pressure of 175/90 mm. Hg, and subsiding erythema along the right saphenous vein. No enlargement of the nodes, liver, or spleen was felt. The results of neurological examination were normal. The chest as examined by roentgenogram was normal.

Laboratory Data.—The results of urinalysis showed no abnormalities except for the presence of urobilinogen in dilutions up to 1:1,000. The blood urea nitrogen value was 16 mg. per 100 cc. of serum, total amount of cholesterol was 193 mg. per 100 cc. of serum, the total protein level was 5.80 gm. per 100 cc. of serum with an albumin fraction of 3.37 gm. and

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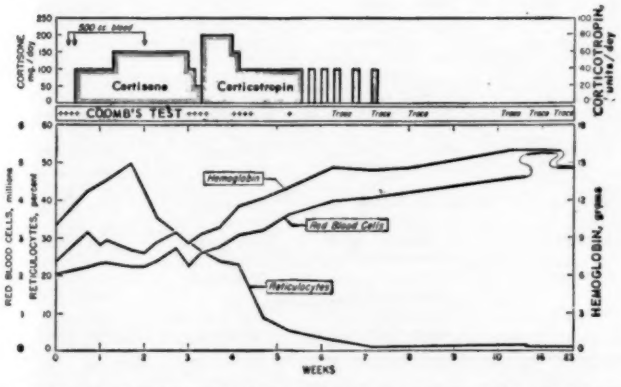
From the Swedish Hospital.

1. Dameshek, W., and Rosenthal, M. C.: Symposium on Specific Methods of Treatment: Treatment of Acquired Hemolytic Anemia with Note on Relationship of Periarteritis Nodosa to Hemolytic Anemia, M. Clin. North America 35: 1423-1440, 1951.

2. Meyers, M. C.; Miller, S.; Linman, J. W., and Bethell, F. H.: The Use of ACTH and Cortisone in Idiopathic Thrombocytopenic Purpura and Idiopathic Acquired Hemolytic Anemia, Ann. Int. Med. 37: 352-361, 1952.

2.43 gm. of globulin; the icterus index was 20 units, and a cephalin flocculation test gave a 3+ reaction. The hemoglobin value was 7 gm. per 100 ml. of blood, and there were 2,010,000 red blood cells, 23,000 white blood cells, 225,000 platelets with 33% reticulocytes, a normal differential leukocyte count, and five nucleated red blood cells per hundred white blood cells. Numerous macrocytes and spherocytes were present. A direct Coombs' test gave a strongly positive reaction; the indirect test was negative. Cold agglutinins were present in dilution of 1:4. A test for L. E. cells was negative. The blood group was type A, Rh positive. The red blood cells showed increased fragility in hypotonic saline solution. Examination of the bone marrow revealed increased cellularity and normoblastosis. Subsequent hematological and therapeutic data are shown in the figure.

The patient was given a transfusion of 500 ml. of blood on the 2nd, 3rd, and 12th days after her admission to the hospital. Although no evident hemolysis was observed, no rise in the amount of hemoglobin or the number of red blood cells ensued. The patient was given 50 mg. of cortisone orally twice daily for four days; after this time the dose was increased to 150 mg. a day. The patient was placed on a salt-free diet, and 2 gm. of potassium chloride was given daily. There was no improvement in the blood cell count, and the number of reticulocytes varied from 31 to 50% red cells per cubic millimeter. The number of nucleated red blood cells ranged up to nine per hundred leukocytes. The patient's clinical condition was unchanged



Results of hematological tests made on a patient with idiopathic acquired hemolytic anemia who received cortisone and corticotropin therapy.

except that she complained of precordial pain radiating to the left arm, in addition to previously described symptoms of dyspnea and palpitation. Blood pressure levels ranged from 130/80 mm. Hg to 160/90 mm. Hg. There was no increase in her weight. After 17 days of cortisone therapy, corticotropin was substituted (20 mg. every six hours intramuscularly). After six days 40 units of the gel form were administered daily for 10 days; four additional doses were then given intermittently. Within five days after corticotropin treatment was begun, the amount of hemoglobin and the number of red blood cells began to rise. The number of leukocytes fell to normal levels in 10 days, and nucleated red blood cells were no longer present. The number of reticulocytes dropped to 1% per cubic millimeter or less in one month. After six weeks there were 16 gm. of hemoglobin per 100 ml. of blood and 4,500,000 erythrocytes per cubic millimeter. The results of a hypotonic saline test for fragility of red blood cells were normal after 10 weeks. The direct Coombs' test is still faintly positive at the time of writing, eight months after onset of disease. The icterus index and cephalin flocculation test are normal. All symptoms of cardiac distress have been relieved.

COMMENT

When the adrenal cortex of dogs is stimulated by corticotropin, up to 15 steroids are liberated, chief of which are hydrocortisone (compound F) and corticosterone (compound B).[3] Clinical trial of hydrocortisone in doses of 100 or 200 mg. given daily for treatment of hemolytic anemia has already been carried out by Rosenthal and co-workers[4] in four cases, three of which were associated with chronic lymphocytic leukemia. Responses to the medicament given intramuscularly in two instances were incomplete, a fact thought to be due to poor utilization of hydrocortisone given in this manner. One of two patients receiving oral therapy had a complete remission of symptoms; another responded incompletely but had a good remission when the medication was changed to cortisone.

It is apparent from the foregoing and our own experience that, of the various types of steroid therapy now available for treating acquired hemolytic anemia, corticotropin induces remissions more regularly. The physiological status of the patient's adrenal glands at the time of therapy probably influences the end-result.[5] The patient whose case is described here was evidently resistant to cortisone in what is considered adequate dosage. There may be other steroids produced by the adrenal glands that are more potent in suppressing hemolytic activity. The possibility exists that various types of hemolytic disease may react optimally to different steroids.

ADDENDUM

Since the preparation of this manuscript we have observed another patient with idiopathic acquired hemolytic anemia who failed to respond to cortisone therapy. After splenectomy a temporary remission ensued for about two months and then hemolysis recurred. No response to cortisone treatment in doses up to 200 mg. a day was noted, but remission followed the administration of cortisone parenterally. Unfortunately the patient died of mesenteric thrombosis during the fourth week of corticotropin therapy. (There were 300,000 to 400,000 platelets per cubic millimeter of blood.)

550 E. 16th St. (25) (Dr. Meyer).

3. Zaffaroni, A.: Symposium on Steroids in Experimental and Clinical Practice, White, A., editor, New York, Blakiston Company, 1951, pp. 96-99.

4. Rosenthal, M. C.; Spaet, T. H.; Goldenberg, H., and Dameshek, W.: Treatment of Acquired Hemolytic Anemia with Compound F Acetate, Lancet **1**: 1134-1140, 1952.

5. Liddle, G. W.; Rinfret, A. P.; Island, D., and Forsham, P. H.: Factors Responsible for the Variable Effectiveness of ACTH in Man, read before the American Society for Clinical Investigation, Atlantic City, N. J., May 4, 1953, abstracted, J. Clin. Invest. **32**: 584, 1953.

Humility.—In the effort to take the world as a real place and not evade its reality you may on occasion find wisdom in the art of timing, in taking advantage of the fact that life ebbs and flows, that the work of the world, like the work of the heart, goes on by means of diastole as well as systole, that children pass through phases, that enough is enough, that a sense of humor and proportion has its uses as well as being perfectly delightful. . . . The elder Walpole had a formula for living that you may find useful: "Good sense, good humor, good manners, and good faith." And there's an antidote for self-pity in Christopher Morley's statement that any man who is worth his salt has by the age of 45 acquired his crown of thorns: the problem is to learn how to wear it over one ear. But the greatest aid in creating yourself may come from cultivating the art of criticizing yourself. What is the best school of medicine in the world today? The best school is that whose graduating class not only knows how to criticize themselves but succeed in holding to themselves the magic mirror of humility incessantly, forever interested in learning.—A. Gregg, M.D., Creativeness in Medicine, *Texas Reports on Biology and Medicine*, no. 3, 1953.

PRIMARY TORSION OF THE OMENTUM IN CHILDREN

H. Clinton Davis, M.D.
Martin Mangels, M.D., Miami, Fla.
and
A. A. Bolton, M.D., Fort Lauderdale, Fla.

While primary torsion of the omentum is unusual in adults, it is exceedingly rare in children. When MacLean [1] reviewed the literature in 1950, he found two instances of omental torsion in children and he reported three others from England. In one instance, however, MacLean pointed out that concomitant appendicitis was present and that therefore the case could be considered one of secondary omental torsion. The low incidence of primary torsion in children and the similarity to the clinical picture of acute appendicitis in children make the following case reports of interest.

Summary of Reports of Torsion of the Omentum in Children

Author and Year of Report	Age of Patient (Yr.)	Chief Complaint	Vomiting	No. of White Blood Cells	Operative Procedure	Type of Incision	Result of Operation
Erdmann, J. F.: Ann. Surg. 73: 252, 1921	14	Pain in right side of abdomen	Yes	Not stated	Omental excision Appendectomy (Appendicitis)	Not stated	Not stated
Barsky, E. K., and Schwartz, A. M.: Am. J. Surg. 38: 356, 1937	5	Pain in right lower quadrant of abdomen	Yes	14,400	Omental excision Appendectomy	Right paramedian	Patient recovered
MacLean, 1950 [1]	6	Pain in right lower quadrant	Yes	Not stated	Omental excision Appendectomy	McBurney	Atelectasis, patient recovered
MacLean, 1950 [1]	4	Pain in right lower quadrant	No	Not stated	Omental excision Appendectomy	Not stated	Not stated
MacLean, 1950 [1]	4	Pain in right lower quadrant	Yes	Not stated	Omental excision Appendectomy	Not stated	Not stated
Davis, Mangels, and Bolton, 1953	6	Pain in right lower quadrant	No	17,000	Omental excision Appendectomy	McBurney	Patient recovered
Davis, Mangels, and Bolton, 1953	3	Pain in right lower quadrant	No	18,000	Omental excision Appendectomy	Right paramedian	Patient recovered

REPORT OF CASES

CASE 1.—A 6-year-old white boy was admitted to the hospital for observation because of pain in the right lower quadrant of the abdomen. The child had noticed generalized abdominal pain two weeks before his admission. The pain apparently had subsided, and the patient was asymptomatic until just before admission when he awakened with cramp-like abdominal pain in the lower right quadrant, which increased in severity throughout the day. This pain became localized at McBurney's point. There was no history of vomiting and no abnormality of the stools. The patient had had two normal bowel movements the previous evening. He had had a slight amount of nausea just before examination at the hospital. There was no history of upper respiratory infection. The past history was noncontributory. The physical signs were those of tachycardia, pain in the right lower quadrant, tenderness over McBurney's point, rigidity, and rebound tenderness. When a rectal examination was made, no tenderness and no mass were found. No mass was palpable abdominally. The results of laboratory tests showed 17,000 white blood cells with 90% polymorphonuclear leukocytes. A diagnosis of acute appendicitis was made, and the patient was taken to the operating room where a McBurney incision was made. When the peritoneal cavity was opened, dark, bloody, ascitic fluid was noted. The appendix was not inflamed. A gangrenous portion of omentum with torsion was palpated and excised. At the same time an appendectomy was performed. The pathology report on the excised portions listed hemorrhagic epiploitis and a normal appendix.

CASE 2.—A 3-year-old girl who was obese was admitted to the hospital with a complaint of pain in the right lower quadrant of the abdomen, which had awakened her from a sound sleep. The pain had subsided but when she reawakened in the morning, the patient complained of the same type of pain. The pain again subsided and reoccurred at two to three hour intervals. She had anorexia but did no vomiting, and there was no constipation, diarrhea, or upper respiratory infection present. The child played normally between the occurrence of pains. Physical examination revealed the abdomen to be markedly obese; there was muscle guarding on the right side with slight rigidity. There was a slight tachycardia. There was definite tenderness over McBurney's point. No peristalsis could be heard. The results of urinalysis were normal. The number of white blood cells was 18,050 with 72% polymorphonuclear leukocytes. Although the history was somewhat unusual, a diagnosis of appendicitis was made. When the patient was operated upon, through a right paramedian incision, the findings were bloody ascites and torsion consisting of five twists in the omentum, with hemorrhagic, omental infarction. The serosa of the parietal peritoneum and visceral peritoneum showed mild diffuse inflammatory injection. The operative procedure consisted of excision of the involved omentum and an appendectomy. The pathology report [2] listed hemorrhagic omentum and mild catarrhal change with lymphoid hyperplasia of the appendix.

COMMENT

Primary torsion of the omentum excludes all those instances where the torsion is associated with other pathological conditions of the abdomen, such as adhesion, hernia, or inflammation. Almost all of the 100 reported cases have occurred in the third, fourth, fifth, and sixth decades of life.[3] Although the etiology is not certain, obesity, trauma, excessive activity, hyperperistalsis, and hemodynamic forces have been suggested as possible factors.[4] It is noted that the omentum in children is poorly developed and almost devoid of fat. This may be an explanation of the rarity of omental torsion in children.[1]

The signs and symptoms are variable; usually there is pain that is described as moderate and sometimes "colicky" in nature in the right lower quadrant of the abdomen. Pain on the right side may be explained by the fact that the right half of the omentum is usually longer than the left and unipolar torsion is more apt to occur on the redundant side. Nausea and anorexia are apt to occur although the patient does not vomit. Para-

Attending Surgeons, Variety Children's Hospital (Drs. Davis and Mangels).

1. MacLean, A. B.: Primary Torsion of the Omentum in Children, Brit. M. J. 1: 100, 1950.
2. Rezek, P. R.: Personal communication to the authors.
3. Leitner, M. J.; Jordan, C. G.; Spinner, M. H., and Reese, E. C.: Torsion, Infarction and Hemorrhage of the Omentum as a Cause of Acute Abdominal Distress, Ann. Surg. 135: 103, 1952.
4. Pool, R. M.: Primary Torsion of the Omentum, Am. Surgeon 17: 841, 1951.

lytic ileus may occur if sufficient time has passed. Fever and leukocytosis will vary with the duration of symptoms. Tenderness with rigidity at McBurney's point has been noticed in most instances. At surgery, bloody, dark ascitic fluid will often be found together with the gangrenous, infarcted, edematous omentum.

In most instances the preoperative diagnosis is acute appendicitis, and surgery is rarely delayed because of the severity of the symptoms. The treatment consists of excision of the gangrenous portion of the omentum, and usually a concomitant elective appendectomy is performed.

939 duPont Bldg., Miami, Fla. (Dr. Davis).

MANAGEMENT OF ISONIAZID INTOLERANCE

Emil Rothstein, M.D.
and
Thomas H. Bruce, M.D., Cincinnati

The value of isoniazid in the treatment of tuberculosis has been firmly established.[1] At the present time its most important role lies in the treatment of patients whose bacilli have become resistant to streptomycin, although it is of great value in all active tuberculous infections. Isoniazid is a drug of extremely low toxicity, and acute gastrointestinal symptoms or febrile reactions from its use are extremely uncommon. Nevertheless, two of the patients we have treated recently presented problems in management because of these infrequent symptoms.

REPORT OF CASES

CASE 1.—A 41-year-old man had pulmonary tuberculosis in 1948. He had been treated with pneumoperitoneum for two years and had in addition received streptomycin on several occasions. In 1949 he was given this drug daily for one month. He was given streptomycin alone intramuscularly from October, 1952, until June, 1953. He was also given *p*-aminosalicylic acid, but because of severe gastrointestinal symptoms administration of this drug could not be continued. Isoniazid was prescribed but produced severe gastrointestinal symptoms consisting of nausea, vomiting, diarrhea, and marked faintness and weakness on four different occasions before the patient was admitted to the Veterans Administration Center, Dayton, Ohio, on Aug. 10, 1953.

At the time of admission the chest roentgenogram revealed far-advanced nodular tuberculous lesions bilaterally with one small cavity. Sputum examinations revealed numerous acid-fast bacilli. The patient was given two 50 mg. tablets of isoniazid. Within one-half hour severe cramp-like pain in the abdomen and profuse watery diarrhea developed. These conditions lasted almost 24 hours and produced weakness and dehydration.

An effort was then made to increase the patient's tolerance to the drug. Isoniazid was given intramuscularly, starting with 1 mg. on the first day with the dosage increased according to the following schedule: 1, 2, 3, 5, 8, 10, 15, 25, 50, and 100 mg. per day. This was followed by oral administration of isoniazid in the same dosage. The patient had no toxic symptoms from any of these doses and at the time of writing was taking 100 mg. of the drug three times daily with no untoward symptoms.

CASE 2.—A 41-year-old man had been suffering from asthma for several years and had been acutely ill for two months. At the time of admission to the Veterans Administration Center, Dayton, Ohio, chest roentgenograms revealed pneumonic consolidation of the upper lobe of the right lung, with a huge cavity. The patient was quite toxic. Sputum tests were positive for Mycobacterium tuberculosis. Treatment was begun with streptomycin, 1 gm. twice weekly, *p*-aminosalicylic acid, 12 gm. daily, and isoniazid, 300 mg. daily. Treatment proceeded uneventfully for about one month, after which time severe daily attacks were noted, consisting of a temperature rise to 103 F, dyspnea, cyanosis, and severe vomiting. All chemotherapy was stopped, with complete subsidence of all symptoms. Five days later 100 mg. of isoniazid alone was given. The patient had a temperature of 102 F, profuse vomiting, sweating, dyspnea, and cyanosis. No medicaments were given for four days, and the symptoms disappeared. Administration of 50 mg. of isoniazid was followed by similar but less severe symptoms on two subsequent occasions. "Desensitization" was attempted with oral administration of isoniazid in solution. The daily doses were 1, 2, 3, 5, 7, 10, 13, 15, 20, 25, 35, 50, 100, 200, and 300 mg. These were taken uneventfully, and the patient continued to be successfully treated with the full dosage of 300 mg. daily.

COMMENT

The mechanism whereby the profound symptoms were produced is not known. In our experience with hundreds of patients who were given isoniazid, severe gastrointestinal or acute systemic toxic manifestations were not previously encountered. In the two patients discussed in this report, identical symptoms had been produced on four or five occasions within a few hours after oral administration of isoniazid.

The severity of the diarrhea, dehydration, fever, vomiting, and dyspnea made the use of isoniazid impossible unless the tolerance could be raised. It was felt that isoniazid was necessary for the treatment in these cases in view of the extent and severity of the active far-advanced tuberculosis. The mechanism of "desensitization" or of increasing tolerance is not understood, but a similar type of program has been successful in increasing tolerance to (or "desensitizing" to) *p*-aminosalicylic acid.[2]

42 Oldham Rd., West Newton, Mass. (Dr. Rothstein).

From the Veterans Administration Center, Dayton, Ohio, and the College of Medicine, University of Cincinnati. Dr. Rothstein is now chief, Tuberculosis Service, Veterans Administration Hospital, Brockton, Mass.

1. Control Study of Isoniazid: United States Public Health Service Cooperative Investigation, Dis. Chest **24**: 361 (Oct.) 1953.

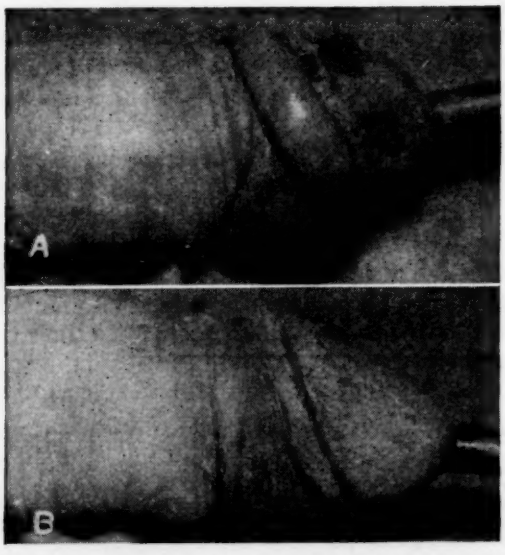
2. Warring, F. C., Jr., and Howlett, K. S., Jr.: Allergic Reactions to Para-Aminosalicylic Acid, Am. Rev. Tuberc. **65**: 235 (March) 1952.

Orphanhood.—Notwithstanding the decline in mortality since the turn of the century, orphanhood is still a sizable problem in our country. Currently, a white child born into a family where the father is only 25 years old has 44 chances in 1,000 of becoming a paternal orphan before reaching its 18th birthday. Moreover, the risk of orphanhood increases with advance in the age of the parent. Thus, the chances of paternal orphanhood rise to 101 per 1,000 if the father is 35 years of age at the birth of the child and to 231 per 1,000 if he is then age 45. However, the incidence of orphanhood is much lower now than 50 years ago for children born to relatively young parents. . . . The chances that a child will lose its mother while it is still a dependent are materially smaller than those of losing its father. Two factors account for this situation: age for age, the death rate is lower for wives than for husbands; furthermore, the wife is generally several years younger than her mate. Yet, under current conditions 40 out of every 1,000 white children born to mothers at age 30 will be maternal orphans before reaching their 18th birthday. The chances increase to 88 per 1,000 when the mother is 40 years old at the child's birth. At the turn of the century the risk of maternal orphanhood was much higher than it is at present.—The Chances of Orphanhood, *Statistical Bulletin Metropolitan Life Insurance Company*, October, 1953.

HYALURONIDASE IN THE TREATMENT OF PARAPHIMOSIS

R. K. Ratliff, M.D., Ann Arbor, Mich.

The best known characteristic of hyaluronidase is its unique ability to disintegrate certain physiochemical barriers of the body. This function has been turned to practical purposes in the use of the drug as a spreading agent in hypodermoclysis, as a local anesthetic, and in the solution of many experimental problems. Recently in our hospital paraphimosis developed in a patient convalescing from a transurethral resection of the prostate gland. A shiny, tense, edematous ring and swelling of the ventral skin were noticed (see figure). Hyaluronidase, 150 turbidity units dissolved in 1 cc. of isotonic sodium chloride solution, was injected and dispersed into the edematous ring at the 3 o'clock and 9 o'clock positions. In 2 minutes the edema took on a pitting quality, and at the end of 12 minutes, when the second picture was taken, the swelling of both the ring and the frenum had completely disappeared and the prepuce was reduced with ease and without pain. The results have been consistently good in four patients, suggesting that the use of hyaluronidase should permanently replace the painful traumatic reduction or the dorsal slit in the correction of paraphimosis.



A, edematous ring and swelling of the ventral skin in paraphimosis before injection of hyaluronidase; *B*, swelling reduced 12 minutes after injection of hyaluronidase.

326 N. Ingalls St.

From the Department of Urology, St. Joseph Mercy Hospital.
Two of the four patients mentioned were treated by Dr. M. L. Ford, Akron, Ohio. The hyaluronidase was supplied by Wyeth, Inc.

Complications of Peptic Ulcers.—The medical aphorism, "Bleeding ulcers do not perforate and perforated ulcers do not bleed," is still quite generally accepted by physicians and surgeons, in spite of rather impressive evidence that both of these disastrous events can occur in the same patient, often at the same time. Although concomitant bleeding and perforated ulcer in the same patient are fortunately rare, the denial of the possibility of their occurrence may cost the life of the patient.—Louis Pelner, M.D., and Walter Puderbach, M.D., Bleeding Ulcers May Perforate, *Postgraduate Medicine*, December, 1953.

PREVENTION OF GANGRENE IN ISCHEMIA OF THE FOOT BY A PROTECTIVE COATING

Meyer Naide, M.D., Philadelphia

The chief problem in managing patients with severe ischemia of the foot is the prevention of gangrene and amputation. Because of the constant presence of the problem of the ischemic extremity with fragile skin that is on the verge of cracking or breaking down, the need for a substance that would protect the skin is evident. The lack of an adequate method of protecting the skin of a patient with ischemia has been a major defect in the program of prevention of gangrene and amputation.

PREPARATION USED AND METHOD

A search was made for a coating that would be simple to apply and protect the ischemic skin. Of a variety of substances tested the most useful proved to be the old preparation, compound tincture of benzoin. Compound tincture of benzoin was available in all hospitals and in almost all offices and was simple to apply. It dried quickly so that clothing could be applied to the areas coated with the substance within five minutes. Furthermore, it was economical.

The compound tincture of benzoin used at first was the U. S. P. preparation, the composition of which, as stated in the Pharmacopeia of the United States, 14th revision, was as follows: benzoin 10%, aloe 2%, storax 8%, and tolu 4% in alcohol, with absolute alcohol content about 80%. As use of this preparation was continued, however, it was found that compound tincture of benzoin as ordinarily made up was too dilute and left too thin a coating. It was found that if one took compound tincture of benzoin as ordinarily made up and evaporated the alcohol until one-half of the original volume was left, one obtained a more concentrated preparation that proved much more useful as a protective coating.

The evaporation was done by placing 80 to 100 cc. of compound tincture of benzoin in a 100 cc. beaker and allowing the alcohol to evaporate spontaneously. It took 24 to 48 hours for the volume to be reduced to one-half. (This could also be done by prescribing 60 cc. of the U. S. P. preparation and advising the patient to leave the bottle uncorked until the volume was reduced to one-half.) A proper concentration of compound tincture of benzoin resulted in a distinct brown film, not a faint tan or light brown or yellow color, when it was applied to the skin.

The substance was applied with an applicator, and the area that required protection was coated. The coating was then allowed to dry, usually less than five minutes. The number of applications varied from 3 to as many as

From the Vascular Section of the Robinette Foundation, Hospital of the University of Pennsylvania, and the Vascular Clinics of the Woman's Medical College of Pennsylvania and the Einstein Medical Center, Southern Division.

20. Usually, the application was made at bedtime for three to five nights. Only the fragile areas were painted, not the entire foot.

RESULTS IN ONE HUNDRED TWENTY PATIENTS

One hundred twenty patients with severe ischemia of the feet have required the use of compound tincture of benzoin as a protective coating during a period of two years. The sites most exposed to pressure, the first and fifth toes and the heels, are the areas that require most frequent protection of the skin. Two-thirds of the amputations resulting from arterial occlusions were due to gangrene of the great toe. However, the foot and leg were frequently traumatized and also required protection with compound tincture of benzoin.

Seven of the 120 patients with extreme ischemia who were treated with compound tincture of benzoin required amputation of the leg. Two of the seven had severe ischemic neuritis without gangrene. The others were patients with the most severe grade of ischemia who had so little blood getting into the feet that it was impossible to maintain viability of the tissues.

It is difficult to estimate how many months of hospitalization and how many extremities were saved by this simple protective measure. Nevertheless, gangrene was prevented in many patients and some extremities were saved as the result of preventing the initial break in the skin without which gangrene will usually not start.

One patient, a diabetic with severe ischemia of both feet, required hospitalization for gangrene of the toes three times for a total of 12 weeks prior to the use of compound tincture of benzoin. Hospitalization was unnecessary, since she was seen at intervals of four to six weeks and compound tincture of benzoin was applied whenever a beginning break in the skin was seen. Compound tincture of benzoin was required to prevent a break in the skin on seven different occasions. I believe this patient has been free from gangrene only because an active method of protecting the skin was used instead of hoping that the skin would not crack open or using wool fat, which would not have been suitable for the purpose. This patient, as do so many diabetic patients, had a tendency to dryness of the skin and callus formation as the result of diabetic neuropathy.

Another patient, with severe ischemia of a foot, had been treated in another hospital with heparin, hexamethonium, bed rest, and an oscillating bed. He came in with a cyanotic and fragile great toe, and a cyanotic and denuded area on the heel. Nothing had been done locally to prevent the toe and heel from becoming gangrenous. He was hospitalized and the most important part of the therapeutic regimen consisted of painting his great toe and heel with compound tincture of benzoin once daily and keeping the heel off the bed. The skin toughened quickly with the protective coating and he was discharged after 13 days. During the following 18 months a lesion did not develop.

Many such patients were seen during the past two years. Compound tincture of benzoin increased the ability to prevent the onset of gangrene in these patients.

COMMENT

The protection of ischemic skin is obviously desirable and an important part of the management of patients with severe peripheral arterial occlusion. The wide availability of a preparation, such as compound tincture of benzoin, that lends itself to such simple and economical application is ideal in the prevention of gangrene. If the feet can be inspected at frequent intervals and the skin protected when it appears in danger of cracking open because of excessive dryness or fragility, gangrene can be prevented in many patients. The coating that this preparation forms is thin but persists for a day or two and can be renewed as often as is necessary by the patient.

Compound tincture of benzoin has been used for many years to prevent bed sores, cracked nipples and fissures of the lips and anus but has not been used for protecting the ischemic skin of the patient with severe arterial disease. Thus far, no sensitivity to this drug has been seen in the 120 patients who were treated.

Contraindications to the use of compound tincture of benzoin are its application over areas of obvious infection and over necrotic ulcers. If there is increasing pain in an area to which compound tincture of benzoin is applied, one should suspect necrosis in that area.

SUMMARY

The use of compound tincture of benzoin is described as a protective coating for ischemic extremities, in which gangrene is threatening as the result of an impending break in the skin. Fragile skin can be protected in a simple and effective manner by coating it with this substance. Ointments, such as wool fat and cacao butter or olive oil, are not protective agents and often do not prevent gangrene, although they are of value in softening excessively dry skin. It has been found that a better protective coating is obtained for this purpose if compound tincture of benzoin is used in a more concentrated form than that described in the Pharmacopeia of the United States.

2034 Spruce St.

Epidemiology of Histoplasmosis.—Although extensive investigations have been conducted during recent years, relatively little is known of the epidemiology of histoplasmosis. . . . Epidemics have been described from such varied sources as pigeon excreta in a water tower, a silo, a cave, chicken houses, a storm cellar and an owl's nest. . . . Histoplasmosis has been observed in dogs, cats, rats, mice, skunks, cattle, horse and kodiak bear. . . . It is difficult to determine whether these animals may serve as a reservoir for the disease in man or whether they become infected from the same source as do humans. Since the spores of fungi, including those of *H. capsulatum,* are . . . lighter than grains of pollen, . . . air-borne infections with these agents may readily affect both man and animals in endemic areas. . . . There are at least four potential routes of dissemination of *H. capsulatum:* (1) sputum; (2) urine; (3) feces, and (4) saliva and vomitus. . . . A study of 68 humans with prolonged household contact with 11 dogs clinically ill with histoplasmosis has not elicited any evidence of spread from the infected animals to man. Although laboratory infections have been reported by others, 42 laboratory workers and animal attendants who have participated in our studies of histoplasmosis over a five year span, with exposures varying from three months to five years, have shown no evidence of active histoplasmosis.—J. A. Prior, M.D.; S. Saslaw, M.D., Ph.D., and C. R. Cole, D.V.M., Experiences with Histoplasmosis, *Annals of Internal Medicine,* February, 1954.

COUNCIL ON FOODS AND NUTRITION

ACCEPTED FOODS

The following products containing non-nutritive artificial sweeteners intended for use in low carbohydrate, low sodium and other therapeutic diets have been accepted as conforming to the rules of the Council. Data regarding composition represent the best available information which is based on submitted reports of analyses. The Council has requested continuing analytical studies, especially of the sodium content of products intended for use in low sodium diets, because of the natural variations in the composition of processed foods.

JAMES R. WILSON, M.D., *Secretary.*

Pratt-Low Preserving Company, Santa Clara, Calif.

Pratt-Low Brand Diet Sweet Dietetic Pack Apricots.

Ingredients: Apricots packed in water without any added sugar or salt.

Analysis (submitted by manufacturer).—Total solids 9.6%, moisture 90.4%, ash 0.6%, fat (ether extract) 0.1%, protein (N × 6.25) 0.5%, crude fiber 0.3%, carbohydrates other than crude fiber (by difference) 8%, sodium 5 mg./100 gm., cyclamate calcium, 0.076%, and soluble saccharin 0.019%.

Calories.—0.37 per gram; 10 per ounce.

Use.—In low calory, low sodium, and other therapeutic diets.

Pratt-Low Brand Diet Sweet Dietetic Pack Pears, Bartlett Halves.

Ingredients: Bartlett pears packed in water without any added sugar or salt.

Analysis (submitted by manufacturer).—Total solids 9.1%, moisture 90.9%, ash 0.2%, fat (ether extract) 0.1%, protein (N × 6.25) 0.2%, crude fiber 0.6%, carbohydrates other than crude fiber (by difference) 7.9%, sodium 2 mg./100 gm., cyclamate calcium 0.057%, and soluble saccharin 0.014%.

Calories.—0.36 per gram; 10 per ounce.

Use.—In low calory, low sodium, and other therapeutic diets.

Pratt-Low Brand Diet Sweet Dietetic Pack Peaches, Yellow Cling, Sliced and Halves.

Ingredients: Yellow cling peaches packed in water without any added sugar or salt.

Analysis (submitted by manufacturer).—Total solids 8.7%, moisture 91.3%, ash 0.3%, fat (ether extract) 0.1%, protein (N × 6.25) 0.4%, crude fiber 0.2%, carbohydrates other than crude fiber (by difference) 7.6%, sodium 4 mg./100 gm., cyclamate calcium 0.064%, and soluble saccharin 0.016%.

Calories.—0.34 per gram; 10 per ounce.

Use.—In low calory, low sodium, and other therapeutic diets.

Pratt-Low Brand Diet Sweet Dietetic Pack Peaches, Elberta Freestone, Sliced and Halves.

Ingredients: Elberta Freestone peaches packed in water without any added sugar or salt.

Analysis (submitted by manufacturer).—Total solids 9.6%, moisture 90.4%, ash 0.4%, fat (ether extract) 0.1%, protein (N × 6.25) 0.4%, crude fiber 0.3%, carbohydrate other than crude fiber (by difference) 8.3%, sodium 4 mg./100 gm., cyclamate calcium 0.08%, and soluble saccharin 0.019%.

Calories.—0.37 per gram; 10 per ounce.

Use.—In low calory, low sodium, and other therapeutic diets.

Pratt-Low Brand Diet Sweet Dietetic Pack Fruit Cocktail.

Ingredients: Pears, peaches, pineapple, grapes, and maraschino type cherries, packed in water without any added sugar or salt.

Analysis (submitted by manufacturer).—Total solids 9.5%, moisture 90.5%, ash 0.2%, fat (ether extract) 0.1%, protein (N × 6.25) 0.3%, crude fiber 0.4%, carbohydrates other than crude fiber (by difference) 8.4%, sodium 4 mg./100 gm., cyclamate calcium 0.064%, and soluble saccharin 0.016%.

Calories.—0.38 per gram; 11 per ounce.

Use.—In low calory, low sodium, and other therapeutic diets.

Pratt-Low Brand Diet Sweet Dietetic Pack Green Gage Plums.

Ingredients: Green Gage plums packed in water without any added sugar or salt.

Analysis (submitted by manufacturer).—Total solids 9.3%, moisture 90.7%, ash 0.3%, fat (ether extract) 0.1%, protein (N × 6.25) 0.4%, crude fiber 0.2%, carbohydrates other than crude fiber (by difference) 8.2%, sodium 2 mg./100 gm., cyclamate calcium 0.076%, and soluble saccharin 0.019%.

Calories.—0.36 per gram; 10 per ounce.

Use.—In low calory, low sodium, and other therapeutic diets.

Pratt-Low Brand Diet Sweet Dietetic Pack Thompson Seedless Grapes.

Ingredients: Thompson seedless grapes packed in water without any added sugar or salt.

Analysis (submitted by manufacturer).—Total solids 14.5%, moisture 85.5%, ash 0.3%, fat (ether extract) 0.1%, protein (N × 6.25) 0.5%, crude fiber 0.2%, carbohydrate other than crude fiber (by difference) 13.3%, sodium 5 mg./100 gm., cyclamate calcium 0.045%, and soluble saccharin 0.011%.

Calories.—0.57 per gram; 16 per ounce.

Use.—In low calory, low sodium, and other therapeutic diets.

Pratt-Low Brand Diet Sweet Dietetic Pack Kadota Figs.

Ingredients: Kadota figs packed in water without any added sugar or salt.

Analysis (submitted by manufacturer).—Total solids 14.2%, moisture 85.8%, ash 0.3%, fat (ether extract) 0.2%, protein (N × 6.25) 0.6%, crude fiber 0.6%, carbohydrates other than crude fiber (by difference) 12.4%, sodium 3 mg./100 gm., cyclamate calcium 0.076%, and soluble saccharin 0.019%.

Calories.—0.56 per gram; 16 per ounce.

Use.—In low calory, low sodium, and other therapeutic diets.

Pratt-Low Brand Dietetic Pack All Green Asparagus.

Ingredients: Mammoth and large spears variety asparagus, packed in water without any added salt.

Analysis (submitted by manufacturer).—Total solids 6%, moisture 94%, ash 0.5%, fat 0.1%, protein (N × 6.25) 2.2%, crude fiber 0.4%, other carbohydrates (by difference) 1.3%, total sugars (as invert) 1.5%, and sodium 7.66 mg./100 gm.

Calories.—0.21 per gram; 6.1 per ounce.

Use.—In low sodium, low calory, and other therapeutic diets.

Pratt-Low Brand Dietetic Pack Cut Blue Lake Beans.

Ingredients: Blue Lake variety green beans packed in water without any added salt.

Analysis (submitted by manufacturer).—Total solids 5%, moisture 95%, ash 0.5%, fat 0.1%, protein (N × 6.25) 1.1%, crude fiber 0.5%, other carbohydrates (by difference) 2.8%, and sodium 9.10 mg./100 gm.

Calories.—0.17 per gram; 5.0 per ounce.

Use.—In low sodium, low calory, and other therapeutic diets.

Pratt-Low Brand Dietetic Pack Spinach.

Ingredients: California variety spinach, packed in water without any added salt.

Analysis (submitted by manufacturer).—Total solids 7.1%, moisture 92.9%, ash 0.8%, fat 0.2%, protein (N × 6.25) 2.4%, crude fiber 0.7%, other carbohydrates (by difference) 2.2%, total sugars (as invert) 0.8%, and sodium 34 mg./100 gm.

Calories.—0.23 per gram; 6.8 per ounce.

Use.—In low sodium, low calory, and other therapeutic diets.

The following products have been accepted as conforming to the rules of the Council.

JAMES R. WILSON, M.D., *Secretary.*

Snively Groves, Inc., Winter Haven, Fla.

Cypress Gardens Brand Diet Pak Unsweetened Grapefruit Juice.

Ingredients: grapefruit juice packed without added sugar or syrup.

Analysis (submitted by manufacturer).—Total solids 10.5%, ash 0.4%, fat trace, protein (N × 6.25) 0.5%, crude fiber trace, available carbohydrates (other than crude fiber by difference) 9.6%, sodium 1 mg. per 100 gm., and ascorbic acid (minimum when packed) 30 mg. per 100 ml.

Calories.—0.40 per gram; 11.5 per ounce.

Use.—In calory-restricted, carbohydrate-restricted, and sodium-restricted diets.

Cypress Gardens Brand Diet Pak Unsweetened Orange Juice.

Ingredients: orange juice packed without added sugar or syrup.

Analysis (submitted by manufacturer).—Total solids 12.3%, ash 0.5%, fat trace, protein (N × 6.25) 0.7%, crude fiber trace, available carbohydrates (other than crude fiber by difference) 11.1%, sodium 0.5 mg. per 100 gm., and ascorbic acid (minimum when packed) 40 mg. per 100 ml.

Calories.—0.47 per gram; 14 per ounce.

Use.—In calory-restricted, carbohydrate-restricted, and sodium-restricted diets.

Cypress Gardens Brand Diet Pak Unsweetened Blended Orange and Grapefruit Juice.

Ingredients: orange juice and grapefruit juice packed without added sugar or syrup.

Analysis (submitted by manufacturer).—Total solids 10.4%, ash 0.5%, fat 0.2%, protein (N × 6.25) 0.6%, crude fiber 0.1%, available carbohydrates (other than crude fiber by difference) 9.1%, sodium 0.3 mg. per 100 gm., and ascorbic acid (minimum when packed) 35 mg. per 100 ml.

Calories.—0.41 per gram; 12 per ounce.

Use.—In calory-restricted, carbohydrate-restricted, and sodium-restricted diets.

Cypress Gardens Brand Diet Pak Artificially Sweetened Grapefruit Sections.

Ingredients: grapefruit sections packed in grapefruit juice artificially sweetened with non-nutritive cyclamate calcium (Sucaryl).

Analysis (submitted by manufacturer).—Total solids 8.7%, ash 0.4%, fat 0.1%, protein (N × 6.25) 0.6%, crude fiber 0.2%, available carbohydrates (other than crude fiber by difference) 7.5%, sodium 3.3 mg. per 100 gm., ascorbic acid (minimum when packed) 30 mg. per 100 ml., and cyclamate calcium not over 0.5%.

Calories.—0.40 per gram; 11.5 per ounce.

Use.—In calory-restricted, carbohydrate-restricted, and sodium-restricted diets.

Cypress Gardens Brand Diet Pak Unsweetened Grapefruit Sections.

Ingredients: grapefruit sections packed in unsweetened grapefruit juice without added sugar or syrup.

Analysis (submitted by manufacturer).—Total solids 8.7%, ash 0.4%, fat 0.1%, protein (N × 6.25) 0.6%, crude fiber 0.2%, available carbohydrates (other than crude fiber by difference) 7.5%, sodium 3.3 mg. per 100 gm., and ascorbic acid (minimum when packed) 30 mg. per 100 ml.

Calories.—0.40 per gram; 11.5 per ounce.

Use.—In calory-restricted, carbohydrate-restricted, and sodium-restricted diets.

Cypress Gardens Brand Diet Pak Artificially Sweetened Grapefruit and Orange Sections for Salad.

Ingredients: grapefruit sections and orange sections packed in grapefruit juice artificially sweetened with non-nutritive cyclamate calcium (Sucaryl).

Analysis (submitted by manufacturer).—Total solids 10.4%, ash 0.5%, fat 0.2%, protein (N × 6.25) 0.6%, crude fiber 0.1%, available carbohydrates (other than crude fiber by difference) 9.1%, sodium 3.3 mg. per 100 gm., ascorbic acid (minimum when packed) 35 mg. per 100 ml., and cyclamate calcium not over 0.5%.

Calories.—0.43 per gram; 12 per ounce.

Use.—In calory-restricted, carbohydrate-restricted, and sodium-restricted diets.

Cypress Gardens Brand Diet Pak Unsweetened Grapefruit and Orange Sections for Salad.

Ingredients: grapefruit sections and orange sections packed in unsweetened grapefruit juice without added sugar or syrup.

Analysis (submitted by manufacturer).—Total solids 10.4%, ash 0.5%, fat 0.2%, protein (N × 6.25) 0.6%, crude fiber 0.1%, available carbohydrates (other than crude fiber by difference) 9.1%, sodium 3.3 mg. per 100 gm., and ascorbic acid (minimum when packed) 35 mg. per 100 ml.

Calories.—0.43 per gram; 12 per ounce.

Use.—In calory-restricted, carbohydrate-restricted, and sodium-restricted diets.

COUNCIL ON PHYSICAL MEDICINE AND REHABILITATION

APPARATUS ACCEPTED

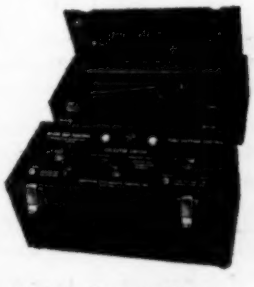
The following additional product has been accepted as conforming to the rules of the Council on Physical Medicine and Rehabilitation of the American Medical Association for inclusion in Apparatus Accepted. A copy of the rules on which the Council bases its action will be sent on application.

RALPH E. DE FOREST, M.D., *Secretary.*

A.C.M.I. Portable Electrosurgical Unit, Model C-350

American Cystoscope Makers, Inc., 1241 Lafayette Ave., New York 59.

The A.C.M.I. Portable Electrosurgical Unit, Model C-350, is a generator of high frequency currents for use in surgery. A source of 50 to 60 cycle alternating current at 115 volts is required for operation and the power consumption is 800 watts. The unit incorporates two distinct circuits: one yields a tube-generated current for cutting; the other utilizes a spark-gap to generate a current for coagulation.



A.C.M.I. Portable Electrosurgical Unit, Model C-350.

The apparatus is contained in a carrying case and measures 35 by 46 by 21 cm. (13½ by 18 by 8½ in.). When packed for shipment it measures 48 by 57 by 38 cm. (19 by 22½ by 15 in.) and weighs 18 kg. (40 lb.). The shipping weight includes the following accessories: footswitch, chuck handle, cord for active terminal, cord for indifferent terminal (with indifferent plate), inlet cable, and a set of eight surgical electrodes.

The Council obtained evidence indicating that this apparatus was satisfactory for minor surgery, such as that performed in an office or clinic on ambulatory patients.

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THE PHYSICIAN AND THE VIRUS DIAGNOSTIC LABORATORY

Much of the material received by a virus diagnostic laboratory consists of specimens from sporadic cases of central nervous system infection, atypical pneumonia, etc. Adair and his associates [1] recently reported the results of virus studies carried out over a period of 11 years of 854 cases of acute aseptic meningitis occurring in military personnel and their dependents in the United States. About 9% of these cases were caused by infection with the virus of lymphocytic choriomeningitis and 12% by the mumps virus. Additional studies of another portion of these patients indicated that the virus of herpes simplex was responsible for about 5% and Leptospira 7%. No specific causative agent was incriminated in about three-fourths of the cases of sporadic aseptic meningitis studied. A similar situation exists in the laboratory diagnosis of atypical pneumonia.

In general, three types of laboratory examinations are used for diagnosis of viral and rickettsial disease: (1) histopathological examination, (2) various serologic tests to detect the presence of specific antibodies, and (3) attempts to isolate the causative agent by chick embryo, animal, and, more recently, tissue culture inoculation. The usefulness of microscopic examination is limited because of the similar pathological lesions produced by many of the viruses, especially those of the neurotropic group. Relatively few viruses produce inclusion bodies that are diagnostic. A notable exception is rabies, because the Negri body is pathognomonic.

The serologic approach is the most practical and depends on the demonstration of a significant rise (fourfold or greater) in antibody titer in serums obtained during the acute and convalescent phases of illness. Serologic tests include the complement fixation, hemagglutination inhibition, and neutralization tests. The disadvantage of the serologic method is that a diagnosis can usually be made only after the disease is well established. Complement fixation is recommended as the serologic test of choice for the routine diagnosis of many viral and rickettsial diseases by the hospital laboratory.[2] Commercial diagnostic antigens and antiserums are now available for many viruses and rickettsias. Certain nonspecific serologic tests are also of considerable aid in diagnosis. These include the heterophil agglutination test for infectious mononucleosis and cold hemagglutination and Streptococcus MG agglutination for atypical pneumonia.

The neutralization test is very useful and fairly accurate but is too technical, costly, and time consuming for the small hospital laboratory because animals or fertile eggs are needed. Furthermore, there is also considerable risk of laboratory infection in working with many of the viruses and rickettsias in the active state. The neutralization test is used to identify a newly isolated virus or to detect the presence of antibody in the patient's serum. Blood specimens for complement fixation, hemagglutination inhibition, or neutralization tests must be properly collected according to the directions of the virus laboratory. Whole blood must not be refrigerated before removing the serum if the cold agglutination test is to be done. Serum specimens may be stored in the refrigerator at 4 C for several days without significant loss of complement fixing antibody titer. Each specimen tube must be carefully labeled with the patient's name, clinical diagnosis, physician's name, date of onset of illness, and date the specimen was drawn. In all serologic tests a diagnosis should not be made from results obtained with a single serum specimen. The positive result may be due to past infection (anamnestic reaction) or previous vaccination. Acute phase serum should be collected as soon as possible after onset of illness (preferably before the fifth day) and convalescent phase serum two weeks after onset. A third serum specimen may be necessary from four to eight weeks after onset. Negative or weakly positive reactions in the acute phase followed by either a positive reaction or a fourfold or greater rise in antibody titer are diagnostic. Close liaison must be maintained between the clinician and the laboratory so that the proper battery of diagnostic antigens will be selected for test, depending on the history and clinical observations; for example, serum from a suspect virus pneumonia patient is tested with the following complement fixing antigens: influenza A, A′, B, and C, psittacosis, and Q fever. In addition, the serum may be tested for the presence of cold and Streptococcus MG agglutinins.

Animal and chick embryo inoculation may afford considerable information in diagnosis but is a research procedure that is expensive, time consuming, and possibly dangerous. Highly trained and skillful personnel are required. The specimens collected depend on the clinical diagnosis and include blood, spinal fluid, nasopharyngeal washings, stool, etc. At autopsy blocks of tissue are removed aseptically from various parts of the body, depending on the cause suspected. Specimens should be collected in sterile, rubber-stoppered vials that are carefully labeled and stored in dry ice until they are ready for animal or chick embryo inoculation. Duplicate blocks of each tissue should also be obtained for pathological study. In the collection of material for virus or rickettsial isolation, it must be emphasized that many of these agents are unstable and rapidly become inactivated at room tem-

1. Adair, C. V.; Gauld, R. L., and Smadel, J. E.: Aseptic Meningitis, a Disease of Diverse Etiology: Clinical and Etiologic Studies on 854 Cases, Ann. Int. Med. 39:675, 1953.

2. Milzer, A.: Routine Laboratory Diagnosis of Virus and Rickettsial Diseases: Results of an 18-Month Study, J. A. M. A. 143:219 (May 20) 1950.

perature but retain their infectivity if stored at low temperatures. A complete case history should accompany all specimens. If a virus is isolated, the laboratory must be prepared to prove that the virus recovered was isolated from the patient and does not represent a natural or accidental virus infection of the stock animals or a laboratory contamination. If the hospital laboratory is unable to conduct viral or rickettsial studies, other laboratories set up to carry out such tests that might be contacted include local city and state health departments; U. S. Public Health Service, Communicable Disease Center Virus and Rickettsia Laboratory, Montgomery, Ala.; and the Department of Viral and Rickettsial Diseases, Army Medical Department, Research and Graduate School, Washington 12, D. C.

The introduction of simplified tissue culture techniques by Enders and his associates [3] and the HeLa strain of malignant human epithelial cells by Syverton and his associates [4] have increased the possibilities of a wider range of virus diagnostic tests as well as the isolation of new viruses. For example, by the use of the tissue culture technique, it is now possible within a few days to isolate and type the poliomyelitis virus from the stool of a patient suspected of having the disease.[5] Several new viruses [6] have been isolated recently from patients that are pathogenic only for tissue culture of human or monkey origin, while standard laboratory animal and chick embryo inoculation with these agents have given negative results.

SUNGLASSES AND THE SOLAR ECLIPSE

On June 30, 1954, there will be a total solar eclipse similar to the one of a decade ago. This will be of great interest to a large part of the population, many of whom may try to view the eclipse through colored glass, so-called sunglasses, or other colored or tinted devices. This practice can be very harmful, and the public should be warned against it.

The Joint Committee on Industrial Ophthalmology of the American Medical Association and the American Academy of Ophthalmology and Otolaryngology has investigated the field of filter lenses and has issued a statement that so-called sunglasses (more correctly called sport glasses) do not have a chemical composition that filters out the harmful sun rays, i. e., infra-red. Men in the armed forces who served as spotters are reported to have had for this reason macular burns with permanent loss of central vision. During the last solar eclipse there were other cases of the burning of the macula with loss of central vision.

The Joint Committee on Industrial Ophthalmology issued a statement [1] that should interest almost all physicians. In substance, the committee asserted visual acuity cannot be improved appreciably by wearing tinted lenses; sunlight of even high intensity will not produce discomfort in some persons, but if discomfort does exist it may be diminished by wearing sunglasses; the use of colored lenses by that part of the population (at least 5%) that does not have normal color perception may exaggerate their defects and cause trouble, for example, when colored traffic signals are viewed against the bright background of a sunset. The committee said the primary function of a sunglass is to reduce brightness. The committee also pointed out that brightness can be reduced by wearing a visor or broad-brimmed hat, which frequently will obviate the necessity of sunglasses, that any type of "night-driving" lens reduces the total light transmitted to the eye and makes seeing more difficult at night, that colored windshields may prove a hazard at night, and that the continual use of sunglasses may reduce the wearer's tolerance to bright light.

The committee believes that tinted lenses are useful in the presence of photophobia due to pathological conditions but that in the absence of disease they should not be prescribed. Of particular interest in view of the solar eclipse is the committee's statement "no commercially marketed sunglass is sufficiently dense to permit direct gaze at the sun." The public should be warned of this, and the medical profession must be on the alert to give such information to all persons who might be encouraged to make use of it. Macular burns with permanent loss of central vision is an expensive price to pay to satisfy a few minutes' curiosity.

THE MAILING OF BLOOD SPECIMENS

It has become a common practice to mail blood specimens collected in glass vials and packed in metal screw-topped containers to private or governmental laboratories for various tests. Basically the postal authorities have no objection to this practice, but complaints have reached the headquarters of the American Medical Association in increasing numbers that the caps of the metal containers are in many instances carelessly screwed on. This results in the glass vial slipping out of the container where it may become broken, so that the specimen stains other mail, to say nothing of the loss to the sender and his patient. In some instances several specimens have come out of their containers in one batch of mail thereby posing an impossible riddle for the postal authorities of trying to figure out which specimen came from which tube. Screwing the caps on securely is apparently not the answer to this problem. Physicians or their technical assistants should place a strip of adhesive tape, preferably not the transparent plastic type, across the top and extending down the sides of the container. A little forethought in this matter will benefit all concerned.

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3. Enders, J. F.; Weller, T. H., and Robbins, F. C.: Cultivation of the Lansing Strain of Poliomyelitis Virus in Cultures of Various Human Embryonic Tissues, Science **109**: 85, 1949. Robbins, F. C.; Weller, T. H., and Enders, J. F.: Studies on the Cultivation of Poliomyelitis Viruses in Tissue Culture: II. The Propagation of the Poliomyelitis Virus in Roller-Tube Cultures of Various Human Tissues, J. Immunol. **69**: 673, 1952.

4. Syverton, J. T.; Scherer, W. F., and Elwood, P. M.: Studies on the Propagation in Vitro of Poliomyelitis Viruses: V. The Application of Strain HeLa Human Epithelial Cells for Isolation and Typing, J. Lab. & Clin. Med. **43**: 286, 1954.

5. Robbins, F. C.; Enders, J. F.; Weller, T. H., and Florentino, G. L.: Studies on Cultivation of Poliomyelitis Viruses in Tissue Culture: V. Direct Isolation and Serologic Identification of Virus Strains in Tissue Culture from Patients with Nonparalytic and Paralytic Poliomyelitis, Am. J. Hyg. **54**: 286, 1951. Syverton and others.[4]

6. Robbins, F. C., and Weller, T. H.: Application of Tissue Culture Methods to the Study of Viral Infections, Pediatrics **13**:283, 1954.

1. Tinted Optical Media, Report of Subcommittee of the Joint Committee on Industrial Ophthalmology, Indust. Med. **21**: 129 (March) 1952.

ORGANIZATION SECTION

LOUISIANA STATE MEDICAL SOCIETY

Although the Louisiana territory was claimed for France by Robert Cavalier de La Salle in 1682 and was transferred from France to Spain and from Spain to France again, medical progress did not start until the territory had been purchased by the United States in 1803. In "A Review of Louisiana Medical Literature, 1796-1843, the Formative Years," William D. Postell, M.S., points out: "Up to the time of the Louisiana Purchase in 1803, very little was done by the French and Spanish governments to provide medical care for the inhabitants of the Mississippi Valley. The founding of the Charity Hospital at New Orleans in 1736 and the decree issued by Governor Alexandro O'Reilly in 1770 relative to the practice of medicine in the colony are about the only bright spots in the medical history of the colonial period." That decree laid down regulations

Hutchinson Memorial Building, Tulane University School of Medicine, in which are the headquarters of the Louisiana State Medical Society.

for the practice of medicine and surgery and stipulated that ". . . all pretended healers, who are not provided with documents and certificates, will be punished with imprisonment and arbitrary punishment if they are caught abusing the credulity of the people; all the so-called bearers of secrets will be dealt with in the same way; believing it impossible for a man of rectitude to hold back knowledge useful to humanity. . . ." Surgeons, after being accepted for practice, were forbidden to "practice any mechanic art or public business under penalty of forfeiting their privileges."

Immediately after the American occupation of the colony, attempts were made to improve sanitary conditions. The legislature was asked to make laws to enforce cleanliness and to subject the shipping entering the Mississippi River to quarantine regulations. That such measures were urgently needed is attested by the fact that, of 935 troops that had been stationed in New Orleans for the protection of the city, 638 became ill and 240 died during the 47 day period when their camp was being moved to a spot eight miles below the city.

The state of Louisiana was admitted to the Union in 1812, but as early as 1804 a notice appeared in the *Louisiana Gazette* that a medical society was to be organized. No records exist to prove that these plans were then carried into effect. In 1808, when there were about 18 physicians in the Parish of Orleans, which had a population of about 17,000, the legislature passed the first act establishing the standards and procedure for physicians in Louisiana. The need for organization became apparent to the physicians of New Orleans when, in 1817, an epidemic of yellow fever raged through the city. Accordingly in 1818 they organized the Société Médicale de la Nouvelle-Orléans. A legislative act was passed authorizing the new organization "to raise by lottery a sum of money not exceeding $15,000 for the purchase of a library, philosophical apparatus . . . and defraying other incidental expenses of the institutions." The society was in existence for four years, was reorganized in 1835, continuing until 1839, was again reactivated in 1859, and continued until 1861. It published a journal at irregular intervals, and certain of its discussions, issued separately, are still extant.

Since the deliberations of La Société Médicale de la Nouvelle-Orléans were in French, in 1820 the English-speaking physicians who were settling in the new state organized their own group called the Physico-Medical Society, "believing that a frequent interchange of opinions on subjects connected with their profession is the most effectual mode to promote its interests and extend their knowledge." The Physico-Medical Society functioned until 1838, was reorganized in 1844, and continued until 1860 or 1861.

Factions within the profession were evidenced by a third medical society, the Louisiana Medico-Chirurgical Society, which was formed in 1843 and continued through 1849. An attempt to make this a state-wide organization is shown by the fact that every licensed physician was made a corresponding member.

Louisiana, following old French law, is divided into parishes instead of counties, and the first parish society, the West Feliciana Medical Society, is said to have been organized in St. Francisville in 1845. This was closely followed by the Attakapas Medical Society from the parishes of St. Mary, Lafayette, St. Martin, and Vermilion. The latter, in conjunction with the Physico-Medical Society, was a prime mover in the formation of the first true Louisiana State Medical Society in 1849. However, the difficulties of travel made state-wide cooperation almost impossible at this time, and after six annual meetings, all held in New Orleans, the society died for want of nonurban support. Other parish societies of this period of which little is known are the Natchitoches Medico-Chirurgical Society (1855), the Medical Association of North Louisiana, organized in Shreveport (1855), the Houma Scientific Association (1859), and the Medical Institute of the Parish of St. Landry (1861).

This was a period of great medical activity in New Orleans. In 1835, the Medical College of Louisiana, now Tulane University of Louisiana School of Medicine, opened its doors, the first medical school in the deep South. In 1844, the *New Orleans Medical and Surgical Journal* appeared. This is now one of the oldest American medical journals in continuous publication, its name having been changed to the *Journal of the Louisiana State Medical Society* in 1953. The first state board of health was established in 1851, by legislative act. The War between the States put an end to medical societies and medical schools in this area. The medical school closed its doors, students and faculty entering the Confederate service as did almost all able-bodied physicians in the state.

In 1867 the New Orleans Medical Association was formed but lasted only until 1870, after making in 1869 an unsuccessful attempt to organize a state society. The New Orleans Medical and Surgical Association, formed in 1873, was followed by the Orleans Parish Medical Society in 1878, the two merging in 1890 under the latter name. In 1878 the present Louisiana State Medical Society also was organized, again largely through the efforts of the Plaquemine Parish Medical Society (1875), the Shreveport Medical Society (1877), and the New Orleans Medical and Surgical Association. At the organization meeting, 106 members were present.

From its inauguration the Louisiana State Medical Society has promoted the public health by the establishment of standards of medical practice, sponsorship of medical legislation regarding sanitation and the control of communicable diseases, and medical care in state hospitals and other institutions. In 1922 the state society acquired ownership of the *New Orleans Medical and Surgical Journal*, until this time under independent management. In later years it has established a plan for voluntary insurance in provision for medical care, has conducted extension courses for rural physicians, and has been active in health education and in cancer control. A history of the Louisiana State Medical Society is in preparation, which will appear as a part of the Rudolph Matas Medical History of Louisiana. In all, 37 parish medical societies and 7 district societies are affiliated with the state society, which now counts 2,025 physicians in its membership list. Its woman's auxiliary numbers 1,072. Meetings are held annually.

Since 1930 the offices of the society have been on the first floor of the Hutchinson Memorial Building of the Tulane University School of Medicine (seen in the illustration), 1430 Tulane Ave., New Orleans 12. On the second floor is the society's library, which, combined with the library of the Orleans Parish Medical Society and the Rudolph Matas Library of Tulane University, contains about 98,000 volumes.

Officers of the society include: president, Dr. Philip H. Jones, New Orleans; president-elect, Dr. Walter O. Moss, Lake Charles; vice-presidents, Drs. Cuthbert J. Brown, New Orleans, W. Kernan Irwin, Baton Rouge, and Max M. Hattaway, New Orleans; secretary-treasurer, Dr. C. Grenes Cole, New Orleans.

COMMITTEE ON MENTAL HEALTH

This is one of a series of brief statements explaining the work of various departments of the American Medical Association. —ED.

A standing committee of the Board of Trustees, the Committee on Mental Health (originally designated the Committee on Nervous and Mental Diseases) was formed in 1952 to advise the board on all matters relating to psychiatry and the related fields of mental health. The Committee considers problems in the area of mental health and studies plans for establishing programs in this field. It works closely with other organizations interested in mental health to develop coordinated programs. It not only serves as a source of information for A. M. A. officers and trustees but also answers or channels requests for information from physicians and lay persons. It cooperates with other A. M. A. councils, committees, bureaus, and departments in matters relating to psychiatry and mental health and indirectly benefits both the public and the profession by working with other organizations to solve problems in this field.

A. M. A. activities in connection with the problems of alcoholism have been organized and directed by the Committee. This work, once handled by a subcommittee of the Commission on Chronic Illness, has been transferred to the Committee on Mental Health. The Committee has also interested itself in the study of effects on human behavior and the administration of justice of crime portrayal in mass mediums. The Committee is now sponsoring a pilot study in a U. S. university in an attempt to determine adequate techniques for the study of these effects that will provide answers free from emotional bias. The question of licensing or legal certification of psychologists has been studied by the Committee. A recommendation by the Committee that the A. M. A. not support such measures was concurred in by the A. M. A. House of Delegates in December, 1952.

A national conference on mental health was sponsored by the Committee in conjunction with the American Psychiatric Association in 1953 to develop a set of objectives and plans for cooperative work with other groups in the field of mental health and for the future work of the Committee with state and county medical associations. A meeting of psychiatrists and persons in the field of physical medicine, co-sponsored by the Committee on Mental Health and the Council on Physical Medicine and Rehabilitation, is being held in 1954 to establish principles for integrating psychiatry and physical medicine in programs of rehabilitation.

STATEMENT BY DR. GEORGE F. LULL ON H. R. 303

The Honorable Arthur V. Watkins, Chairman May 24, 1954
Subcommittee on Indian Affairs
Committee on Interior and Insular Affairs
United States Senate
Washington, D. C.

Dear Senator Watkins:

I would like to take this opportunity on behalf of the American Medical Association to respectfully submit for your consideration our views concerning H. R. 303, 83rd Congress, which is now pending before your Committee.

This bill, which is designed to provide for the transfer of the functions, responsibilities and duties of the Department of the Interior and the Bureau of Indian Affairs relating to the health and hospitalization of Indians to the United States Public Health Service, has the active approval of the American Medical Association. It is the belief of the Association that the transfer of such facilities to the United States Public Health Service would result in much needed improvements in the health facilities and hospitals available to the Indian population of the United States. Administration of these installations by the Public Health Service would facilitate the recruitment of necessary physicians and allied health personnel and would insure a higher degree of medical care for the beneficiaries of the program.

The position of the Association in this regard was established by the Board of Trustees during the 82nd Congress and reiterated by the Board on February 6, 1953. I therefore urge, on behalf of the Association, that the subject legislation be reported favorably by your Committee.

Sincerely yours,
GEORGE F. LULL, M.D.
Secretary and General Manager.

FEDERAL MEDICAL LEGISLATION

Extension of Social Security Benefits

Congressman Reed (R., N. Y.), in H. R. 9366, introduced the administration's "Social Security Amendments of 1954" with some modifications made by the Ways and Means Committee in the House. This measure replaces H. R. 6812 and H. R. 7199, previously reported, and is essentially similar to these bills. However, in the final form of H. R. 9366, as passed by the House, physicians are not included under compulsory coverage in social security. In computing benefits, the worker's earnings for the lowest four years would be dropped. If he has been employed 20 or more quarters, the lowest 5 years of pay will be dropped. This obviously would eliminate medical determinations of disabilities, except in cases in which disabilities exceed four or five years. The pension rights of a disabled person are protected if he furnishes proof of disability that is medically determinable and exists for six months or more. H. R. 9366 extends until Sept. 30, 1955, the present formula for federal payments to states for public assistance to the aged, blind, disabled, and dependent children. This measure passed the House by a vote of 355 to 8 and has been referred to the Senate Committee on Finance.

Extension of Medical Care for Veterans

Congressman Jarman (D., Okla.) proposes in H. R. 9233 to extend medical, hospital, and domiciliary care of the Veterans Administration to the U. S. citizens who served in active military service in any government allied with the United States in World War II, who, at the time of entrance into such active service, had citizenship of the United States and retained U. S. citizenship. This bill was referred to the Veterans Affairs Committee.

Prepared by the Washington Office of the American Medical Association.

MEDICAL NEWS

CALIFORNIA

Cranks' Calls and Letters.—The Health Department of the City of Los Angeles reports that a "deadly game" is being played by a small antimedicine group, whose targets are parents searching for dogs that bit their children. Following press descriptions of the possibly rabid animals, parents are besieged by anonymous nuisance calls, the telephone is tied up for long periods of time, and they become fearful they will miss the call from someone who has located the biting dog. Dr. George M. Uhl, city health officer, states that "because they also fear violence from the callers, who berate physicians, decry the Pasteur treatment, and even deny the existence of rabies, they permit the crank calls to continue. One family received, in addition to the interminable phone calls, more than 50 crank letters. Not only do the callers sometimes insult parents, but they also frighten the child, whom they often ask for by name when placing the call."

DISTRICT OF COLUMBIA

Philip Murray Clinic.—Providence Hospital has received a check for $150,000 from the Philip Murray Memorial Foundation to be used for a clinic in the new building. It will be named after the late president of the CIO.

Personal.—At the annual commencement of Georgetown University, June 7, Dr. Thomas F. Keliher, clinical associate professor of medicine, Georgetown University Medical Center, Washington, D. C., received the Bene Merenti medal awarded annually in recognition of outstanding service to Georgetown. Dr. Keliher, who joined the university's medical school faculty shortly after receiving his degree there in 1934, has held his present rank since 1945.——At the annual meeting of the Georgetown University Alumni Association, Dr. A. Magruder MacDonald was honored for distinguished service to the country, the city, and his alma mater. Dr. MacDonald, a past president of the Medical Society of the District of Columbia, is District coroner. For many years he was a lecturer on medical jurisprudence at Georgetown University and the National Police Academy of the Federal Bureau of Investigation.——Dr. William R. Stovall, immediate past president of the Aero Medical Association, recently received the association's Theodore C. Lyster award, given annually for outstanding achievement in the general field of aviation. He was recognized for his contribution to the field of civil aviation medicine, particularly for his leadership in obtaining recognition of aviation medicine as a specialty.——The Georgetown Clinical Society has presented to Dr. James A. Gannon its award of merit for his long and distinguished service to medicine. Dr. Gannon served in the department of medicine at Georgetown University School of Medicine, Washington, D. C., from 1908 to 1932. He served as vice-president of the District of Columbia Board of Education from 1940 to 1952, since 1940 has been chairman of the board of draft appeals, and last year was made a member of the Council of Thirteen, which advises the Commissioners on Civil Defense. ——Dr. Donald R. Sickler succeeds Dr. Vernon M. Padgett as head of the division of tuberculosis of the District of Columbia Health Department.

FLORIDA

Miami Heart Institute.—The Miami Heart Institute (4701 N. Meridian Ave., Miami Beach) is equipped to care for patients with cardiac disease, both acute and ambulatory, and also for certain other ambulatory patients, such as those with diabetes, ulcers, hypertension, and cerebral palsy. A registered A.D.A. dietitian supervises all diets. The institute maintains a hotel for guests and relatives of the patients. Dr. E. Sterling Nichol is medical director, Dr. Robert J. Boucek, director of research, and Dr. Harrison A. Walker, director of medical public relations.

ILLINOIS

Shock Therapy for Inmates of Penal Institutions.—The attorney general of Illinois recently advised the director of the Illinois department of public safety that the state of Illinois has authority to administer shock treatments to insane inmates of its penitentiaries. The attorney general advised that such treatment can be administered without the necessity of obtaining consent from the next of kin of the insane prisoner or from someone legally responsible for him. He stated: "It would appear that the authority to use shock treatment may be implied from the meaning inherent in the concept of custody and treatment and the accepted signification of such terms."

First Eisendrath Scholarship Awarded.—Dr. Pierre Chaumont of Paris, France, has been chosen as the first Eisendrath scholar. The scholarship, founded in memory of Dr. Daniel N. Eisendrath, who died in Paris in 1939, and his wife, the late Maude R. Eisendrath, is available each year to a young French graduate of the University of Paris Faculty of Medicine. It permits him to come to the United States for a year's postgraduate study. Dr. Eisendrath was connected with the Cook County and Michael Reese hospitals, Chicago, before moving to Paris, where he was associated with the American Hospital and the Pasteur Institute. He was the author of several books, including "Urology," "Surgical Diagnosis," and "Clinical Diagnosis." Dr. Eisendrath was a Knight of the French Legion of Honor. The scholarship is awarded by the Eaton Foundation on the recommendation of the medical faculty of the University of Paris, to whom all requests for information should be sent.

Chicago

Workshop Seminars in Rorschach Test.—The department of psychology, University of Chicago, announces two workshop seminars in the Rorschach Test, July 6-10 and July 12-16, to be conducted by Samuel J. Beck, Ph.D. Workshop 1, Basic Processes, may be taken by students at, or ready for, the intern level. Admission to Workshop 2, Advanced Clinical Interpretation, is limited to psychologists and psychiatrists in clinical positions or practice. For information write to the Executive Secretary, Department of Psychology, University of Chicago, Chicago 37.

Edward Lorenzo Holmes Award.—The Institute of Medicine of Chicago has established the Edward Lorenzo Holmes award and memorial lecture under the provisions of the trust fund of the late Dr. Rudolph Holmes, which creates the "Rudolph Wieser Holmes and Maria Baxter Holmes Fund" as a memorial to Dr. Edward Lorenzo Holmes, Chicago ophthalmologist, 1828-1900, father of Rudolph Holmes. The income from this fund is to be used for prizes and awards for distinguished contributions to medical science, preference being given to contributions in ophthalmology, especially those made by investigators under 35 years of age. Dr. Arnall Patz, Baltimore, has been selected as the first recipient because of his experimental work on several species of animals reproducing the clinical and histological findings of retrolental fibroplasia by means of high concentration of oxygen.

Personal.—Dr. Vincent J. O'Conor, professor of urology, Northwestern University Medical School, has been invited to address the British Association of Urological Surgeons at the annual meeting in Dublin, Ireland, June 24. The subject of his address will be "The Present Status of Radioactive Isotopes in the Treatment of Carcinoma of the Prostate." He will also discuss "Injuries of the Genito-Urinary Tract" before the Irish Medical Association at Killarney, July 8.——Dr. Edwin L. Crosby, who on June 1 became executive director of the American Hospital

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

Association, Chicago, was awarded an honorary doctor of science degree by his alma mater, Union College, Schenectady, N. Y., at ceremonies in Memorial Chapel, June 13. Dr. Crosby was adjunct professor of public health administration, Johns Hopkins University School of Medicine, and director of the Johns Hopkins Hospital in Baltimore before becoming the first director of the Joint Commission on the Accreditation of Hospitals in 1952.

Veterans Administration Research Hospital.—The new 16 million dollar 500-bed Veterans Administration Research Hospital, the latest addition to the Northwestern University Medical Center, occupies the block bounded by Huron and Erie streets and Fairbanks and McClurg courts on the Chicago campus. The 17-story building was recently dedicated. The two top floors provide space for 46 resident physicians, and floors 9 to 15 are occupied by patients. Each floor, with space for about 80 patients, is made up of two wings of 16 single beds and two wings of six four-bed wards. The 15th floor has been set aside for care of neuropsychiatric patients. On the 10th floor one of the wings has been designed especially for the treatment of patients by means of radioisotopes, and on the ninth floor one

Veterans Administration Research Hospital.

wing is designed as a metabolic ward and general diagnostic ward. The entire eighth floor is devoted to research and contains biochemical, bacteriological, physiological, and biophysical laboratories, and animal quarters. The entire sixth floor is devoted to food preparation and dining facilities for patients and staff. The fourth floor contains an auditorium, chapel, canteen, and other special services, the only strictly medical facility being the department of physical medicine. Operating rooms occupy part of the third floor. Forty per cent of the third floor is devoted to medical education with locker room space for both medical and nursing students. There are five classrooms with a capacity of about 50 and an auditorium. Half of the second floor is devoted to therapeutic equipment and half to diagnostic radiological equipment. The hospital is to be used for teaching junior and senior medical students as clinical clerks.

The medical school is offering a new residency in allergy in connection with the new hospital. The resident will be in charge of a service at the hospital and spend half of his time at the medical school in clinics and research. The service will begin July 1. Applications should be made to Dr. Samuel M. Feinberg, 303 East Chicago Ave., Chicago 11.

KENTUCKY

Society News.—A public relations course for physicians' secretaries, developed by the Education Campaign Committee of the Kentucky State Medical Association, was recently presented for members of Henderson and Daviess County medical societies.

University Appointments.—The University of Louisville announces new faculty appointments, including Dr. Ernest R. Seitz, Veterans Administration Hospital, Louisville, as assistant professor of radiology and Dr. Walden R. Smith as assistant professor of anesthesiology in the department of surgery. Three new sections have been established in the department of medicine: (1) cardiovascular diseases, with Dr. Herbert L. Clay Jr. as chief; (2) diseases of the chest, with Dr. Oscar O. Miller as chief; and (3) gastroenterology, with Dr. Samuel A. Overstreet as chief. Dr. John P. Bell has been promoted from associate to assistant professor of psychiatry; Dr. Joe L. Lawson from instructor to assistant professor of medical psychology in the department of psychiatry; and Dr. Charles H. Crudden from instructor to assistant professor of psychiatry.

LOUISIANA

Dr. Akenhead Made Professor of Medicine.—Dr. Walton R. Akenhead, associate professor of medicine, has been promoted and named to succeed Dr. Edgar Hull as head of the department of medicine at Louisiana State University School of Medicine, New Orleans. Dr. Akenhead joined the LSU medical faculty in 1940. During World War II he served as chief of medical service at Camp Claiborne Station Hospital. In addition to teaching duties, Dr. Akenhead has been director of the Student Health Service of the School of Medicine since April 1, 1946.

MASSACHUSETTS

Society News.—At the annual meeting of the Middlesex South District Medical Society, exercises were held in honor of the completion by Dr. Alexander A. Levi, Boston, of 25 years as secretary of the Middlesex South District Medical Society and his elevation to the presidency. He was presented with a bronze plaque. Other officers chosen were Dr. Ralph H. Wells, Lexington, president-elect, and Dr. David C. Dow, Cambridge, secretary.

Personal.—Dr. Sidney S. Lee has been appointed assistant director and administrator of the outpatient department at Beth Israel Hospital, Boston. Dr. Lee has been on active duty with the U. S. Public Health Service since 1950.——S. Stephen Chapman, Ph.D., instructor in the department of bacteriology and immunology, Harvard Medical School, Boston, has been appointed associate professor of microbiology at the University of Louisville (Ky.) School of Medicine, effective July 1.

Biophysics Research Laboratory.—Harvard Medical School and Peter Bent Brigham Hospital, Boston, announce the opening at the hospital of a Biopsysics Research Laboratory of the Department of Medicine that has as its chief interest the study of "trace elements" in biology and medicine. It is equipped for work in biophysics, biochemistry, and physical chemistry. Biochemical and biophysical approaches will be combined wherever possible. Training facilities are provided for predoctoral and postdoctoral students in the natural sciences and medicine.

Dr. Weller Named First Richard Strong Professor.—Dr. Thomas H. Weller, associate professor of tropical public health, Harvard School of Public Health, Boston, has been named first Richard Pearson Strong professor of tropical public health, the first endowed professorial chair at the school. The new professorship is a memorial to the late Dr. Richard Pearson Strong (1872-1948), professor of tropical medicine at Harvard, who pioneered in tropical medicine research both at Harvard and in the U. S. Army Medical Corps. Endowment funds for the professorship, raised by friends and colleagues of Dr. Strong, included a gift from the Belgian government and a gift from a group of health officials and employees of the government of the republic of the Philippines.

MICHIGAN

Health Officer Needed.—The city of Marquette is seeking a full-time health officer to fill the post, previously held by Dr. Charles P. Drury until his retirement in 1953, which has subsequently been held on a part-time basis by Dr. Andrew L. Swinton. Candidates may communicate with J. A. Clulo, City Manager, Marquette.

Personal.—Dr. Marion W. Jocz has been appointed medical director of Chrysler Corporation to succeed Dr. John J. Prendergast, who has retired after nearly 18 years in that position. Dr. Jocz, who has been affiliated with the company since 1941 and has served as assistant medical director since 1945, will be succeeded in that post by Dr. Louis W. Staudt, who joined Chrysler Corporation in 1950.

MISSOURI

Physicians Needed at Scout Camp.—Physicians are needed for the medical service at the Boy Scout camp at Osceola for the periods July 26 to Aug. 1, Aug. 5 to Aug. 10, and Aug. 10 to Aug. 15. A screened cabin, with shower, toilet, and hot and cold water, is provided, next to the hospital. Physicians who wish to volunteer their services may call Dr. C. Stewart Gillmor, Kansas City, Ba. 2032, or the executive office, Je. 8432.

University News.—Dr. Otakar Machek, instructor in orthopedic surgery, has been appointed to a full-time position in the department of rehabilitation, St. Louis University School of Medicine. Dr. Machek, a native of Czechoslovakia, was awarded a fellowship in physical medicine and rehabilitation at New York University Medical Center before coming to Missouri in 1951 as director of Miriam Rosa Bry Convalescent Rehabilitation Hospital in Webster Grove.

Summer Camps for Diabetic Children.—The St. Louis Diabetes Summer Camp at Camp Lions Den (12½ miles south of St. Louis on U. S. Route 21) has been reserved from Aug. 16 to Sept. 5 by the Lions Council of Greater St. Louis, Boys and Girls Committee, and the St. Louis Diabetes Association, for the use of diabetic children between the ages of 10 and 16. There will be a counselor for every five or six children, a resident physician and nurse, and a dietitian especially trained in preparing diabetic diets. Specialists from St. Louis will visit the camp three times weekly. Information may be obtained from the St. Louis Diabetes Association, 3839 Lindell Blvd.——The Diabetes Lay Society of Greater Kansas City (P. O. Box 8463, Delmar 1844) will accept children aged 7 to 14 for the fourth annual camp for diabetic children at Camp Hope in Swope Park, Aug. 1 to 12. The enrollment fee, $35, includes food, insulin, and medical and nursing care. The camp furnishes an educational and recreational program for the juvenile diabetic under close medical and dietetic supervision. Physicians who have diabetic patients in this age group are requested to notify the society so that information concerning the camp may be forwarded to the parents.

MONTANA

General Practitioners Meet in Lewistown.—The Montana chapter of the American Academy of General Practice will hold its annual meeting at the Elks Lodge in Lewistown, June 26, under the presidency of Dr. John W. Schubert, Lewistown. The guest clinicians are Dr. Nathan E. Silbert, Lynn, Mass., who will present "Management of the Allergic Nose," Dr. Robert B. Greenblatt, Augusta, Ga., "Functional Uterine Bleeding," and Dr. Manuel E. Lichtenstein, Chicago, "Biliary Tract Dysfunction." Mr. C. G. Manning, professor of education, sociology, and economics at Rocky Mountain College, Billings, will have as his topic "Has Medical Science Become Too Scientific?" There will be an informal dance at 10 p. m. The registration fee, $15, will include attendance at the scientific meeting and cocktail and banquet tickets for the physician and his wife. Hotel reservations may be secured from the secretary of the academy, Dr. Harry R. Soltero, 315 N. Broadway, Billings.

NEW JERSEY

County Society Sponsors Public Forum.—Over 1,400 laymen attended the public medical forum sponsored by the Camden County Medical Society, April 23 to 25. During the three day session, 28 exhibits were shown, 418 survey chest roentgenograms were taken, and over 300 specimens of urine were tested for sugar in a diabetic detection survey.

NEW YORK

Camp Physician Wanted.—A position as camp physician is available at the Boy Scout Camp Ti-Wa-Ya-Ee, near Holland. The camp season is two months long, and the position can be divided between two or even more physicians willing to serve part of that time, provided that their services could be made consecutive. Family living quarters are available at the camp, and an additional stipend of at least $500 has been set aside for the two months. For information, telephone Dr. Alfred Golden, Buffalo, UN. 9200, Ext. 229. Pl. 6485.

Personal.—Dr. Joseph T. Doyle, director, Cardiovascular Health Center, Albany Medical College, returned recently from Naples, Italy, where he assisted Ancel B. Keys, Ph.D., director of the Laboratory of Physiological Hygiene at the University of Minnesota, Minneapolis, in his investigation of the relation between the fat content of the diet and the incidence of coronary heart disease. The team of researchers included Dr. Paul D. White, Harvard Medical School, Boston, three cardiologists from Sweden, one from South Africa, one from England, and one from Yugoslavia.

Tri-County Medical Day.—The medical societies for the counties of Wyoming, Genesee, and Livingston will hold their 1954 Tri-County Medical Meeting and Outing in Warsaw, June 24. At 10 a. m. at the Wyoming County Community Hospital, Warsaw, a panel discussion "Recent Advances in Diagnosis and Treatment" will be presented, with Dr. Samuel Sanes, Buffalo, as moderator and Drs. Louis L. Klostermyer, Asheville, N. C., Percy E. Ireland, Toronto, Canada, and L. Maxwell Lockie, Buffalo, among the collaborators. Luncheon at the hospital will follow a question and answer period. Golf will begin at 1 p. m. at the Silver Lake Country Club, where dinner will be preceded by a cocktail party at 6 p. m. A cordial invitation is extended to physicians of Erie County and all Western New York, with their wives and families, to join in the meeting and outing. Special entertainment has been planned.

New York City

Medicolegal Course.—A course in "Medical Testimony in Malpractice and Negligence Cases for Practitioners of Medicine, Law, and Allied Professions" will be given for the first time by the Post-Graduate Medical School of the New York University-Bellevue Medical Center in cooperation with New York University School of Law. Under the direction of Dr. Maxwell H. Poppel, chairman, department of radiology, NYU College of Medicine, the sessions will be held every Thursday, Oct. 7, 1954, through March 10, 1955, 8:30 to 10 p. m. Emphasis will be placed on various aspects and pitfalls of medical testimony in malpractice and negligence cases. Mock trials, question-and-answer periods, and other features simulating actual court conditions will be presented. Members of the department of radiology, as well as judicial and other qualified officials, will participate. Applications may be made through the Office of the Dean, NYU Post-Graduate Medical School, 477 First Avenue, New York 16. Tuition is $100.

OHIO

Science in Law Enforcement.—An Institute on Science in Law Enforcement will be held in Cleveland, June 21 to 26, for law enforcement officers. This will be a cooperative activity of the School of Medicine, School of Law, and the Institute of Pathology of Western Reserve University, and the Cuyahoga County Coroner's Office and Laboratory. Information may be obtained concerning the institute from Oliver Schroeder Jr., Director, The Law-Medicine Center, Western Reserve University, Cleveland 6.

Health Commissioners Needed.—The Ohio Department of Health announces that there are a number of opportunities in Ohio for physicians as health commissioners. In some instances a choice of location is available. The policy of the department permits further academic training of physicians who wish to make a career of public health or prepare themselves for membership in the American Board of Preventive Medicine. Physicians are invited to communicate with the Ohio Department of Health, Bureau of Local Services, 306 Ohio Departments Bldg., Columbus 15.

Richard Allison Memorial.—The Academy of Medicine of Cincinnati recently dedicated a bronze plaque at Third and Lawrence streets, where, just east of Fort Washington, Dr. Richard Allison, Surgeon to the Legion, built his "Peach Grove" house about 1795. Dr. Allison was a veteran of the American Revolution and the Indian wars, having risen from surgeon's mate to ranking medical officer and surgeon to the Legion of the United States. After retirement from the Army in 1796, he continued to practice medicine in Cincinnati and in Clermont County, where his quiet courtesy is said to have endeared him to people in every rank of frontier life. The inscription on the plaque is as follows: "He was an ornament to his profession. . . . In his bounty, distress found relief and in his generosity, unfortunate merit found refuge. Erected in honor of the first physician and surgeon in this vicinity by the Academy of Medicine of Cincinnati."

OKLAHOMA

Society News.—Dr. Roscoe L. Pullen, dean of the University of Missouri School of Medicine, Columbia, will be guest speaker for the Tulsa Academy of General Practice, June 28, 6:30 p. m. at Hotel Tulsa. All physicians are invited to hear him discuss "Trends Influencing Medical Practice." Dinner reservations should be made through the Academy offices (phone 2-5904). The scientific program will be at 8 p. m.

RHODE ISLAND

Personal.—John E. Farrell, Sc.D., executive secretary of the Rhode Island Medical Society, was recently named president-elect of the New England Health Education Association.

State Medical Election.—New officers of the Rhode Island Medical Society, elected at the 143rd annual meeting of the organization, are: Dr. Henri E. Gauthier, Woonsocket, president; Dr. John G. Walsh, vice-president; Dr. Frank B. Cutts, president-elect; Dr. Thomas Perry Jr., secretary; and Dr. John A. Dillon, treasurer, all of Providence.

TENNESSEE

Residency in Ophthalmology.—Dr. Henry Carroll Smith, head, division of ophthalmology, announces that the Vanderbilt University School of Medicine, Nashville, now offers a residency in ophthalmology. Applicants should address him at 630 Doctors Building.

Personal.—When Dr. John C. Burch, professor of obstetrics and gynecology at Vanderbilt University School of Medicine, Nashville, was elected president of the Southern Surgical Association in December, he was escorted to the chair by his father, Dr. Lucius E. Burch, who was president of the association in 1929. ——Dr. Otis S. Warr, a director of the Memphis Heart Association and the Memphis-Shelby County Tuberculosis Association, has been named president of the Civitan Club in Memphis.

University News.—The University of Tennessee College of Medicine, Memphis, announces the appointment of Dr. Oscar M. Derryberry, Chattanooga, director of health for the Tennessee Valley Authority, as lecturer in preventive medicine, and of two Memphis physicians, Dr. Jerome M. Swarts and Dr. Bennett E. Everett Jr., as assistant professor of medicine and instructor in obstetrics and gynecology, respectively.——A portrait of the late Dr. Conley Hall Sanford, who was chief of the division of medicine, University of Tennessee College of Medicine, Memphis, until his retirement in October, 1953, was presented to the college, Feb. 12. Dr. Sanford, who had served the college in varying capacities from 1920 until his retirement, at which time he was chief of staff of John Gaston Hospital, died Nov. 16.

TEXAS

Discussion of Biological Techniques.—On June 30, Chauncey D. Leake, Ph.D., executive director, University of Texas Medical Branch, Galveston, will address a joint meeting of the St. Joseph Valley Chemical Society and the Elkhart County Medical Society at the Miles-Ames Research Institute, Elkhart, on new discoveries with new biological techniques.

Narcotic Violation.—Dr. Blaise Lionel Duhe, 1487 Louisiana St., Beaumont, was convicted in the U. S. District Court at Beaumont of violating the federal narcotic law. On Dec. 21, 1953, he was sentenced to a term of three years each on three separate counts to run concurrently and was fined $500 each on three separate counts. His sentence was suspended, and he was placed on probation for four years.

Personal.—Dr. Bruce D. Fallis, instructor in physiology and biochemistry at the University of Texas Medical Branch, Galveston, has been awarded the 1954 Sarah Mellon Scaife fellowship in pathology at the University of Pittsburgh. Dr. Fallis, first recipient of the fellowship, which was established in 1953, received the Jackson-Johnson scholarship and the Moseby scholarship book award at Washington University School of Medicine, St. Louis, and two university scholarships during his undergraduate work at Texas Christian University, Fort Worth. ——Dr. Harvey B. Snyder, formerly chief resident in medicine at Jefferson Davis Hospital, Houston, and a consultant in electrocardiography at the Houston Veterans Administration Hospital, has joined the medical division of Humble Oil & Refining Company in Houston, as internist and diagnostician.——James P. Cooney, Brigadier General, Commandant, Medical Field Service School, Brooke Army Medical Center, Fort Sam Houston, gave the annual Alpha Omega Alpha lecture at the University of Texas Medical Branch, Galveston, May 14. General Cooney presented "The Physician's Responsibility in Modern Warfare."

WISCONSIN

Personal.—At a dinner at which the village of Footville honored him for 42 years of devoted, friendly service to the community, Dr. James R. Harvey was presented with an engraved silver plaque on behalf of the State Medical Society of Wisconsin.

Conference on Alcoholism.—Educational, social, and scientific developments in the field of alcoholism will be discussed at the 1954 University of Wisconsin Conference on Alcohol Studies, June 20 to 25, on the university campus in Madison. The conference is sponsored by the University of Wisconsin Extension Division in cooperation with the Wisconsin State Bureau of Alcohol Studies and the Wisconsin Council on Alcoholism. The enrollment fee, exclusive of room and meals, is $35.

Memorial Library Dedicated.—The new $1,100,000 Carey memorial library addition to the Marquette University School of Medicine, Milwaukee, was formally dedicated, May 22, and named in honor of the late Dr. Eben J. Carey, who was dean of the school, and the late Mrs. Helene M. Carey who, with Marquette medical alumni, made the library possible with their contributions. Highlighting Dedication Week there was a two day conference on hemorrhagic diseases, which included among its participants Dr. Tage Astrup of the Carlsberg Foundation, Copenhagen, Denmark; Dr. Alfredo Pavlovsky of the Naval Hospital, Buenos Aires, Argentina, and professors from Columbia, Harvard, Johns Hopkins, Marquette, Michigan, Missouri, North Carolina, Syracuse, Tufts, Utah, Wisconsin, and Yale. A $5,000 grant from the Milwaukee Froedtert Foundation made the conference possible.

GENERAL

World Health Organization Adopts Budget.—Rejecting the $10,300,000 recommended by its committee on program and budget, the Seventh World Health Assembly in Geneva has adopted a budget of $9,500,000 for 1955, an increase of 1 million dollars over the 1954 budget. The budget will be financed by assessments totaling $8,550,000 against member states, plus an income of $950,000.

Warning About Photographer.—According to the American College of Surgeons, a St. Louis fellow of the college reported having received a telephone solicitation from a photographer who stated that the "Nationwide Photo Service . . . was going all over the United States photographing fellows" so that the college headquarters would have a picture of each member on file. Such solicitation has not been authorized by the college.

Institute of Acarology.—The Institute of Acarology will be held at the University of Maryland, College Park, from June 21 to July 10. Since the inception of this program at Duke University, Durham, N. C., in 1951, it has provided opportunity for entomologists, parasitologists, and zoologists to learn about mites and ticks. Information can be obtained from George W. Wharton, Department of Zoology, University of Maryland, College Park, Md.

WHO Elects President.—At the opening session in Geneva, Switzerland, May 4, the seventh World Health Assembly elected Dr. Joseph Nagbe Togba, director of public health and sanitation in Liberia, as president. Dr. Togba received his degree of doctor of medicine from Meharry Medical College, Nashville, Tenn. He was one of the vice-presidents of the fifth World Health Assembly and is a retiring member of the World Health Organization Executive Board.

American-Korean Foundation.—Dr. Howard A. Rusk, director, Institute of Physical Medicine and Rehabilitation, New York University-Bellevue Medical Center, has been elected president of the American-Korean Foundation, a nonprofit organization of which Milton S. Eisenhower, D.Sc., president, Pennsylvania State College, State College, Pa., is honorary chairman. The foundation has made cash allocations and grants of goods-in-kind totaling $3,200,000 to Korea in the last eight months of 1953. The foundation's offices are at 345 E. 46th St., New York 17.

General Practice Scholarships.—During the annual scientific assembly of the American Academy of General Practice in Cleveland, the following interns, who will begin their residencies in general practice in July, were announced as winners of $1,000 Mead Johnson General Practice Scholarship awards: Walter Scott Chisholm Jr., St. Luke's Hospital, Denver; Dale Brenton Snow, Southern Baptist Hospital, New Orleans; John Basil Neal, St. Vincent's Hospital, Jacksonville, Fla.; Robert E. Sotta, U. S. Public Health Service Hospital, Norfolk, Va.; and Ocie Carl Yarbrough, Parkland Hospital, Dallas, Texas.

Brochure on Water Fluoridation.—The St. Louis Medical Society has published and made available for purchase the report of its Water Fluoridation Committee, prepared after extensive study of experiments with water fluoridation in numerous communities. Nine tables are reproduced, and a bibliography containing 67 references is appended. The 16 page pamphlet may be obtained from the society at 3839 Lindell Blvd., St. Louis. Single copies up to 10 are 75 cents each. The scale of charges for quantity orders ranges from $6 for 10 copies to $200 for 1,000. Dr. Willard Bartlett, St. Louis, is chairman of the Water Fluoridation Committee which compiled the report.

Request for Enucleated Eyes.—The Uveitis Laboratory, Medical Research Department of Ophthalmology, University of California Medical Center, San Francisco 22, requests all physicians to send freshly enucleated eyes from patients who had diffuse uveitis, iridocyclitis, and chorioretinitis for cultural and pathological studies. The eye, not set in Formalin, should be placed in a sterile bottle and sent as quickly as possible, air express collect, to Dr. Michael J. Hogan, Director, Francis I. Proctor Foundation for Research in Ophthalmology. A complete report will be sent on each specimen received. The laboratory would also like to obtain Formalin-fixed specimens of similar eyes for microscopic study.

Borden Awards.—Borden awards of a gold medal and $1,000 were recently presented to George H. Hart, M.D., V.M.D., dean, University of California School of Veterinary Medicine, Davis, for contributions in the fields of dairy cattle diseases and animal nutrition; Dr. Jean R. Oliver, distinguished service professor, State University of New York College of Medicine at New York City, Brooklyn, and director, Renal Research Unit, Overlook Hospital, Summit, N. J., for accomplishments in the field of kidney research; and Dr. Lawson Wilkins, associate professor of pediatrics, Johns Hopkins University School of Medicine, Baltimore, for studies in the diagnosis and treatment of endocrine disorders in infants and children.

Research Grants in Multiple Sclerosis.—Dr. Harold R. Wainerdi, medical director of the National Multiple Sclerosis Society, 270 Park Ave., New York 17, announces that five new research projects, totaling $22,950, have been approved by the medical advisory board of the society. Grantees include: (1) Albert Schatz, Ph. D., professor of microbiology, National Agricultural College, Bucks County, Pa., the co-discoverer of streptomycin; (2) Pinckney J. Harman, Ph. D., assistant professor of anatomy, New York University College of Medicine; (3) Harry H. Sobotka, Ph.D., Mount Sinai Hospital, New York; (4) Drs. Eli Robins and David E. Smith, assistant professor of psychiatry and assistant professor of pathology, respectively, Washington University School of Medicine, St. Louis; and (5) Dr. Paul Thygesen, Copenhagen, Denmark.

Publications on Alcoholism.—The National Committee on Alcoholism announces publication of the 1953 Directory of Out-Patient Alcoholism Clinics, which lists state, county, city, and privately sponsored outpatient facilities. The publication may be ordered from the National Committee on Alcoholism, 2 E. 103d St., New York 29. Single copies are 25 cents; on orders of 100 or more the price is 15 cents a copy.——A new 70 page booklet, entitled "Alcoholism: A Personal and Community Problem," is being distributed by the North Carolina Alcoholic Rehabilitation Program. The booklet is a compilation of the lectures given at the 1952 Summer Studies on Facts About Alcohol at the University of North Carolina in Chapel Hill. A copy may be obtained free on request from N. C. Alcoholic Rehabilitation Program, Box 9118, Raleigh, N. C.

Foundation Announces Awards.—The National Foundation for Infantile Paralysis has announced approval of research and professional education projects totaling $1,873,485, of which $902,248.30 was allocated for research in prevention of the disease and for improved methods of treatment, and $971,236.70 for programs in professional education. The awards were made to 30 medical schools, hospitals, research institutions, and educational organizations, the highest awards going to Dillard University, New Orleans, ($200,000) under the direction of Albert W. Dent, LL.D., president, and the University of Buffalo School of Medicine ($191,466) under the direction of Dr. Stockton Kimball, dean. The new awards bring to $53,080,224.86 the amount provided in March of Dimes funds since 1938 for the study of medical care problems, aid to professional education, support of poliomyelitis research, and prevention of the disease.

Society News.—Newly elected officers of the **American Academy of Orthopaedic Surgeons** include Dr. T. Campbell Thompson, New York, president; Dr. Walter P. Blount, Milwaukee, president-elect; Dr. Harold E. Crowe, Los Angeles, vice-president; Dr. Jesse T. Nicholson, Philadelphia, treasurer; Dr. John R. Norcross, Chicago, secretary; and Dr. Claude N. Lambert, Chicago, librarian-historian.——Officers of the **New England Obstetrical and Gynecological Society** for 1954 include: Dr. Edward F. Shay, Fall River, Mass., president; Dr. Lewis P. James, Hartford, Conn., vice-president; Dr. Frederick L. Good, Boston, treasurer; and Dr. Carmi R. Alden, Boston, secretary.——At the meeting of the **Society for Pediatric Research** in Buck Hill Falls, Pa., Dr. Charles A. Janeway, Boston, was elected president; Dr. Wolfgang W. Zuelzer, Detroit, vice-president; and Dr. Sydney S. Gellis, Boston, secretary-treasurer.

Traffic Safety Honor Awards.—For going through the entire year of 1953 without a single traffic fatality, 817 cities with more than 5,000 population have won places on the Honor Roll of the National Traffic Safety Contest. The National Safety Council announces that this is an increase of 18 over the number on the 1952 Honor Roll. The largest no-death city in 1953 was Mount Vernon, N. Y., with a population of 71,899. Hobart, Okla., a city of 5,380 population, which state records show has never had a traffic death since its incorporation in 1901, maintained its perfect record through 1953 for the longest sustained performance among cities of more than 5,000 population. Among cities of more than 10,000, top honors for sustained no-death records went to Belmont, Mass. (27,381), with a record of seven consecutive death-free years. Fairfield, Ala. (13,177) and Midwest City, Okla. (10,166) also had seven consecutive death-free years.

Awards for Rehabilitation Films.—International film awards, to be presented at the sixth World Congress of the International Society for the Welfare of Cripples at The Hague, Netherlands, Sept. 13 to 17, have been announced by the society, which has pioneered in the international nongovernmental circulation of rehabilitation films through its Irving Geist International Film Library. Films will be selected on the basis of the technical accuracy, effective presentation, and world-wide value. To be eligible for the awards, a film must have been produced since the society's fifth World Congress, which was held in Sweden in September, 1951, and must be available for screening in the Netherlands before the sixth congress. Nominations should be sent to the International Society for the Welfare of Cripples, 127 E. 52nd St., New York 22. A full description of the film should be included, together with information concerning the production and distribution rights and availability for screening.

One-Act Play on Infantile Paralysis Available.—The National Foundation for Infantile Paralysis has made available a booklet containing script and discussion guide for "New Fountains," a one-act play, produced by the American Theatre Wing Community Plays in collaboration with the foundation and now released for amateur production throughout the country. It is described as "a warm, vital drama, devised to help audiences gain new insight into the needs and problems of the physically disabled." Any community group throughout the country (with the exception of those within a 50 mile radius of New York City) may produce the play with amateur or professional casts. Performing rights within New York City and within a radius of 50 miles thereof are reserved for the professional casts of the American Theatre Wing Community Plays, 351 W. 48th St., New York. Telephone: COlumbus 5-6638. Requests for the booklet should be addressed to: The National Foundation for Infantile Paralysis, 120 Broadway, New York 5.

American Gastroscopic Society.—The annual session of the American Gastroscopic Society will be open to all interested physicians in the Room of the Dons at the Mark Hopkins Hotel, San Francisco, at 5 p. m., June 20. Dr. Edward B. Benedict, Boston, will open a discussion of "Massive Haemorrhage from Gastritis." Dr. Alvin J. Cox, San Francisco, will discuss "The Histological Appearance of Gastritis with Comments on the Possible Clinical Significance of the Condition"; Dr. Paul H. Holinger, Chicago, "The Management of Foreign Bodies in the Oesophagus and Stomach"; and Dr. Rudolf Schindler, Los Angeles, "Gastroscopic Observations in Post-Operative Stomachs." A cocktail party will precede the annual banquet, at which Dr. Schindler will give "The Story of the Building of the Flexible Gastroscope." Dr. Schindler will also present for the first time the society's Rudolf Schindler award to the person who, in the opinion of a committee, has done most to advance the gastroscopic method.

Passano Foundation Award.—Homer W. Smith, Sc.D., professor and chairman, department of physiology, New York University College of Medicine, has been selected as the recipient of the $5,000 Passano Foundation award for 1954, which will be presented at a dinner at the St. Francis Hotel, San Francisco, June 21. Dr. Walter B. Martin, Norfolk, Va., President-Elect of the American Medical Association, and Dr. Arthur L. Bloomfield, professor of medicine emeritus, Stanford University School of Medicine, San Francisco, will be among the speakers. Dr. Smith's work has formed the basis for the several kidney function tests and has led to the development of surgical techniques which have insured the success of many routine kidney operations. The Passano Foundation, which was formed late in 1943 to encourage medical science and research, particularly that having a clinical application, is sustained by annual contributions from the Williams & Wilkins Company, publishers of medical and science books.

Announce Faculty Award Winners.—The Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y., has bestowed Lederle Medical Faculty awards on the following physicians:

Don Wayne Fawcett, department of anatomy, Harvard Medical School, Boston, 3 years.
Fred V. Lucas, department of pathology, University of Rochester, 2 years.
George E. Murphy, department of pathology, Cornell University Medical College, 3 years.
James Robert Teabeaut II, department of pathology, University of Tennessee, 1 year.

These awards (THE JOURNAL, June 5, 1954, page 586) are intended to strengthen the preclinical departments of medical schools in the United States and Canada by contributing to the support of the teaching and research activities of members of such departments who already have demonstrated high quality of performance but have not yet attained permanent faculty tenure.

Fellowships for Medical Students.—The National Foundation for Infantile Paralysis announces that fellowships will continue to be available in 1954 for medical students who have completed at least two years of medical school work and who have eight weeks of consecutive free time to devote to extracurricular study. The stipend will be $400. Three types of fellowships will be offered: (1) research in the basic sciences related to medicine, (2) physical medicine and rehabilitation, and (3) public health and preventive medicine. Deans of medical and basic science schools are invited to nominate one candidate for the research fellowship and two candidates for each of the other fellowships. Since the purpose of these programs is to enable the student to determine his own ability and aptitudes early in his career, no student who has an equivalent orientation will be eligible. For further information and for application forms, students should consult with the deans of their respective schools. Applications should be submitted to the National Foundation for approval at least eight weeks before the beginning of the program.

Transport Deaths.—According to a study by the World Health Organization, presenting data collected in 15 countries on deaths resulting from transport accidents on land and sea and in the air, up to half of all young persons who die between the ages of 15 and 24 are killed in traffic accidents, motor vehicles are responsible for more than 70% of all transport deaths, and children are their chief victims. The study analyzes 22 types of transport accidents under six main headings: (1) railway accidents; (2) motor vehicle traffic accidents, including collisions with trains, pedestrians, cyclists, and motorcyclists, as well as accidents without prior collision, caused by swerving, overturning, etc.; (3) motor vehicle nontraffic accidents occurring off the public highway, such as garage accidents and fires; (4) other road vehicle accidents (tramcar accidents, accidents to pedestrians, cyclists, or animals); (5) water transport accidents, resulting in deaths while on board or leaving or boarding ships and boats; and (6) aircraft accidents. A copy of the WHO Epidemiological and Vital Statistics Report is available at the UN press documents counter in the United Nations, N. Y.

Therapeutic Society Invites Papers.—The American Therapeutic Society, which will hold its 55th annual meeting at the Chase Hotel, St. Louis, Nov. 4 to 7, invites its members to submit the titles of papers on new and interesting subjects, together with a 200-word abstract in quadruplicate, to the program committee before July 1. The society also announces that two awards will be given for outstanding work in therapeutics: the Lewis H.

Taylor lectureship, which has been given for some years, and the new Oscar B. Hunter memorial award which, initiated with this meeting, will be presented to the physician who has made the most outstanding contribution to therapeutics during the preceding years. Nominations for the lectureship and the award are solicited. The council of the society, which has furnished the fund necessary to finance the first award, feels that many members of the society may desire to be associated with the perpetuation of this award. This will be made possible by the establishment of a separate fund. Contributions may be sent to the treasurer, Dr. Howard Wakefield, 122 S. Michigan Ave., Chicago.

Trachoma Practically Eliminated in U. S.—Trachoma, an infectious eye disease causing intense pain and blindness, has been practically eliminated in the United States through the use of modern drugs, Dr. Kingsley W. Cosgrove of Little Rock, Ark., reported March 12 before the annual conference of the National Society for the Prevention of Blindness in St. Louis. At one time there were 75,000 cases in the United States. Dr. Cosgrove reported that treatment with sulfonamides and other drugs has reduced the incidence of the disease to the point at which it is "no real problem." He pointed to Arkansas as an example of the gains that have been made. There was an annual total of 1,736 new cases of trachoma reported in Arkansas as recently as 1940; in 1952, the total was only 10. Before introduction of the sulfonamides, there was a high incidence of trachoma among American Indians. The sulfonamide treatment, Dr. Cosgrove said, reduced the disease from 22% among Indian school children in 1944 to barely 0.25% by 1952. In Illinois there were 2,416 cases in 1949; in 1953 no new cases were reported. In Oklahoma, where the incidence of trachoma had been "historically high," of 3,000 school children screened for symptoms, only 2 were found to be suffering from the disease.

Vascular Surgery Meeting.—The Society for Vascular Surgery will hold its annual meeting at the Mark Hopkins Hotel, San Francisco, June 20. The sessions will begin at 9 a. m. with the presentation "The Comprehensive Surgical Management of Cavernous Hemangiomas of the Lower Extremity with Special Reference to Stripping" by Drs. Joseph M. Janes and Thomas T. Myers, Rochester, Minn. Immediately preceding the executive session luncheon (for members only), Drs. Harold A. Zintel, Charles C. Wolferth, William A. Jeffers, J. A. Mackie, and Stephen B. Langfeld, Philadelphia, will report on "Experiences with Thoracolumbar Sympathectomy and with Combined Adrenalectomy—Sympathectomy in the Treatment of Patients with Essential Hypertension." After the presidential address by Dr. Michael E. DeBakey, Houston, Texas, 2 p. m., Dr. Lawrence N. Atlas, Los Angeles, will discuss "The Application of the Principle of 'Hemometakinesia' to the Technique of Lumbar Sympathectomy." The scientific session will close with a paper, entitled "Pliable Plastic Tubes as Aortic Substitutes," by Drs. Harris B. Shumacker Jr., Indianapolis, Edmond J. Harris, Muncie, Ind., and Harry Siderys, Indianapolis. A cocktail party for members, wives, and guests will precede the annual banquet.

Conference of State Society Officers.—The Conference of Presidents and Other Officers of State Medical Associations will convene for the 10th annual meeting at 1:45 p. m., June 20, in the Gold Ballroom, Palace Hotel, San Francisco, under the presidency of Dr. Louis M. Orr, Orlando, Fla. Dr. Percy E. Hopkins, Chicago, will open the program with "Spheres of Medicine," after which the following panel discussion on doctors and the press will be presented:

From a Magazine Editor's Point of View, Mr. Steven M. Spencer, associate editor of the *Saturday Evening Post*.

From a Science Writer's Point of View, Mr. Alton L. Blakeslee, Associated Press.

From a Physician's Point of View, Herbert P. Ramsey, co-chairman, A. M. A. Committee on Blood, and president, Medical Society of the District of Columbia.

At 3:10 p. m. Mr. Robert L. Stearns, director, Boettcher Foundation, Denver (former president of the University of Colorado), will have as his topic "Are Public Relations Programs Worth What They Cost?" "Our Common Aims" will then be considered by Mr. James Mussatti, general manager, California State Chamber of Commerce, San Francisco. The Armour Laboratories, Chicago, will be host at a reception and cocktail party for officers of state medical associations and their wives at 5:30 p. m.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories, and possessions from Jan. 1 to May 29, 1954:

New England States	
Maine	2
New Hampshire	5
Vermont	1
Massachusetts	27
Rhode Island	2
Connecticut	10
Middle Atlantic States	
New York	114
New Jersey	17
Pennsylvania	54
East North Central States	
Ohio	114
Indiana	19
Illinois	38
Michigan	81
Wisconsin	26
West North Central States	
Minnesota	41
Iowa	27
Missouri	34
North Dakota	7
South Dakota	15
Nebraska	12
Kansas	28
South Atlantic States	
Delaware	..
Maryland	4
District of Columbia	3
Virginia	25
West Virginia	26
North Carolina	42
South Carolina	20
Georgia	57
Florida	250
East South Central States	
Kentucky	34
Tennessee	28
Alabama	67
Mississippi	47
West South Central States	
Arkansas	55
Louisiana	61
Oklahoma	42
Texas	409
Mountain States	
Montana	38
Idaho	15
Wyoming	8
Colorado	19
New Mexico	9
Arizona	25
Utah	21
Nevada	8
Pacific States	
Washington	46
Oregon	36
California	620
Territories and Possessions	
Alaska	46
Hawaii	129
Puerto Rico	16
Total	2,880

Tobacco Industry Cancer Research.—In furtherance of its investigation of the effects of tobacco smoking, the Tobacco Industry Research Committee has invited university, hospital, and other medical research organizations throughout the nation to submit proposals for specific cancer research projects for consideration by the committee's Scientific Advisory Board. An initial fund of $500,000 for research has been appropriated by the committee, which is composed of major cigarette manufacturers, tobacco growers, and warehousemen. On the advice of

the Scientific Advisory Board, this committee has also pledged to vote substantial additional funds for specific projects. The tobacco industry, it is said, will not set up any research facilities but will conduct its long-term research program in institutions outside the industry. No industry funds will be given to tobacco company laboratories. The committee invites (1) information concerning facilities and personnel available for the production of such research and (2) suggestions from qualified investigators for the specific planning of projects. Suggestions for research should be sent to Dr. Clarence Cook Little, The Tobacco Industry Research Committee, 5400 Empire State Bldg., New York 1. The other members of the advisory board are: Dr. McKeen Cattell, professor of pharmacology, Cornell University Medical College, New York; Dr. Leon O. Jacobson, professor of medicine, University of Chicago School of Medicine, and director of the Argonne Cancer Research Hospital, Chicago; Dr. Paul Kotin, assistant professor of pathology, University of Southern California School of Medicine, Los Angeles; Dr. Kenneth Merrill Lynch, president, Medical College of the State of South Carolina, Charleston; Dr. Stanley P. Reimann, scientific director of the Institute for Cancer Research, Philadelphia; and Dr. William F. Rienhoff Jr., associate professor of surgery, Johns Hopkins University School of Medicine, Baltimore.

LATIN AMERICA

Campaign Against Yaws.—Until 1950 yaws affected about one-third of the rural population of Haiti and 50% of the inhabitants in some areas. In a campaign waged by the Haitian government with the aid of the World Health Organization and the United Nations International Children's Emergency Fund between July, 1950, and Dec. 31, 1953, 2,623,141 persons were treated with penicillin. Recent surveys revealed that less than one-third of 1% of the population now has contagious yaws.

FOREIGN

Congress of Neurologists and Psychiatrists.—A Congress of Neurologists and Psychiatrists of the French-speaking countries will convene in Liege, Belgium, July 26 to 31. Symposiums will be presented on myasthenia gravis, traumatic neuroses, and treatment of chronic alcoholism. All physicians are invited to attend. Those who have communications related to myasthenia gravis are requested to contact Dr. Pierre Passouant of the Faculty of Medicine, the University of Montpelier, or Dr. J. Radermecker, chief of the Medical Center of Military Psychiatry at Antwerp, Belgium.

Congress of Orthopaedic Surgery and Traumatology.—The International Society of Orthopaedic Surgery and Traumatology will hold its sixth congress at Berne, Switzerland, Aug. 30 to Sept. 3. The principal subjects for discussion are "Treatment of Scoliosis" and "Surgery of the Hand." Drs. Michael L. Mason, Chicago, and Joseph H. Boyes, Los Angeles, will be among those discussing the latter subject. The following symposiums will be presented: Gerontological Problems of Orthopedic Surgery and Traumatology; The Physiological Bases of Maximal Performances in Sport; Physiology and Pathology of Locomotion; Osteoarticulatory Tuberculosis; and Arthrosis of the Hip. Excursions have been planned that include visits to various medical centers in Basle, Berne, Lausanne, Geneva, and Zurich, and a visit to the Jungfraujoch.

Poliomyelitis Conference.—The third International Poliomyelitis Conference will be held Sept. 6 to 10 at the Orthopedic Clinic, University of Rome, Italy, cosponsors of the conference, with the National Foundation for Infantile Paralysis, U. S. A., and the High Commissionary of Hygiene and Health, the National Council of Research, and the National Foundation for Maternity and Child Care, all of Italy. Dr. Chester Keefer, Boston, will participate in the opening discussion on social aspects of poliomyelitis. On Tuesday Dr. James L. Wilson, Ann Arbor, Mich., will serve as moderator for a panel discussion "Systemic Treatment of the Acute Stage with Brain Stem Involvement and Respiratory Failure" and will direct the technical discussion on mechanical devices for respiratory aid. Dr. Thomas Francis Jr., Ann Arbor, Mich., will serve as moderator on Wednesday for the panel discussion on infection and immunity in poliomyelitis, and John F. Enders, Ph.D., will moderate a panel on tissue culture. Panels on rehabilitation and on orthopedics, Thursday, will be moderated by Dr. Jessie Wright, Pittsburgh, and Dr. Paul C. Colonna, Philadelphia, respectively. Dr. Frank R. Ober, Boston, will serve as chairman for the Thursday program on orthopedics. The Friday session will be devoted to trends in poliomyelitis. Dr. Thomas M. Rivers, New York, will give the summary on microbiology and immunization, and Dr. John R. Paul, New Haven, Conn., will deliver the closing paper of the congress, entitled "Future Prospects."

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1954 Annual Meeting, San Francisco, June 21-25.

1954 Clinical Meeting, Miami, Florida, Nov. 29-Dec. 2.

1955 Annual Meeting, Atlantic City, N. J., June 6-10.

1955 Clinical Meeting, Boston, Nov. 29-Dec. 2.

1956 Annual Meeting, Chicago, June 11-15.

AMERICAN GASTROSCOPIC SOCIETY, Mark Hopkins Hotel, San Francisco, June 20. Dr. John Tilden Howard, 12 East Eager St., Baltimore 2, Secretary.

CONFERENCE OF PRESIDENTS AND OTHER OFFICERS OF STATE MEDICAL ASSOCIATIONS, The Palace, San Francisco, June 20. Mr. Theodore Wiprud, 1718 M St. N.W., Washington 6, D. C., Secretary.

NATIONAL MEDICAL ASSOCIATION, Washington, D. C., Aug. 9-13. Dr. John T. Givens, 1108 Church St., Norfolk 10, Va., Executive Secretary.

NEUROSURGICAL SOCIETY OF AMERICA, Grand Hotel, Mackinac Island, Mich., July 21-24. Dr. Lester A. Mount, 700 West 168th St., New York 32, Secretary.

SOCIETY FOR VASCULAR SURGERY, Mark Hopkins Hotel, San Francisco, June 20. Dr. George D. Lilly, 333 Ingraham Bldg., Miami 32, Fla., Secretary.

FOREIGN AND INTERNATIONAL

BRITISH MEDICAL ASSOCIATION, Glasgow, Scotland, July 1-9, 1954. Dr. A. Macrae, B.M.A. House, Tavistock Square, London, W.C.1, England, Secretary.

CONFERENCE OF INTERNATIONAL UNION AGAINST TUBERCULOSIS, Madrid, Spain, Sept. 26-Oct. 2, 1954. Secretariat, Escuela de Tisiologia, Ciudad Universitaria, Madrid, Spain.

CONGRESS OF INTERNATIONAL ASSOCIATION FOR THE PREVENTION OF BLINDNESS, New York, N. Y., U. S. A., Sept. 12-17, 1954. Professor Franceschetti, 2 Avenue Mirmot, Geneva, Switzerland, Secretary-General.

CONGRESS OF INTERNATIONAL SOCIETY OF MEDICAL HYDROLOGY, Vichy and Paris, France, Sept. 26, 1954. For information write: Dr. Giulio Ammirandoli, Via Della Torretta 11, Montecatini Terme, Italy.

CONGRESS OF INTERNATIONAL SOCIETY OF UROLOGISTS, Athens, Greece, April 1955. Prof. Z. Kairis, 25 rue Voukourestiou, Athens, Greece, Secretary-General.

EUROPEAN SOCIETY OF CARDIOVASCULAR SURGERY, Edinburgh, Scotland, July 9-10, 1954. For information address: Mr. A. J. Slessor, Department of Surgery, University New Building, Edinburgh 8, Scotland.

INTER-AMERICAN CONGRESS OF RADIOLOGY, Shoreham Hotel, Washington, D. C., U. S. A., April 24-29, 1955. Dr. Eugene P. Pendergrass, 3400 Spruce St., Philadelphia 4, Pa., U. S. A., Secretary General.

INTER-AMERICAN SESSION, AMERICAN COLLEGE OF SURGEONS, Universidad Mayor de San Marcos de Lima, Lima, Peru, S. A., Jan. 11-14, 1955. Dr. Michael L. Mason, 40 East Erie St., Chicago 11, Ill., U. S. A., Secretary.

INTERNATIONAL ANESTHESIA RESEARCH SOCIETY, Ambassador Hotel, Los Angeles, Calif., U. S. A., Oct. 10-14, 1954. For information write: Dr. T. H. Seldon, 102-110 Second Avenue S.W., Rochester, Minn., U. S. A.

INTERNATIONAL CANCER CONGRESS, Sao Paulo, Brazil, July 23-29, 1954. Prof. A. Prudente, 171 rua Benjamin Constante, Sao Paulo, Brazil, President.

INTERNATIONAL CONFERENCE ON THROMBOSIS AND EMBOLISM, Basle, Switzerland, July 20-24, 1954. Dr. W. Merz, Chief Medical Officer, Gynecological Clinic, University of Basle, Basle, Switzerland, Hon. Secretary.

INTERNATIONAL CONGRESS OF CLINICAL PATHOLOGY, Washington, D. C., U. S. A., Sept. 6-10, 1954. Dr. Robert A. Moore, Washington University School of Medicine, St. Louis 10, Mo., U. S. A., Chairman, Committee on Arrangements.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Barcelona, Spain, Oct. 4-8, 1954. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Ill., U. S. A., Executive Secretary.

INTERNATIONAL CONGRESS ON GROUP PSYCHOTHERAPY, Toronto, Ont., Canada, Aug. 12-14, 1954. Dr. J. L. Moreno, Room 327, 101 Park Ave., New York 17, N. Y., U. S. A., Director of Organizing Committee.

INTERNATIONAL CONGRESS ON GYNECOLOGY AND OBSTETRICS, Geneva, Switzerland, July 26-31, 1954. Dr. H. de Watteville, Maternité Hôpital Cantonal, Geneva, Switzerland, President.

INTERNATIONAL CONGRESS OF HEMATOLOGY, Paris, Sept. 6-11, 1954. Dr. Jean Bernard, 86 rue d'Assas, Paris 6°, France, Secretary.

INTERNATIONAL CONGRESS OF THE HISTORY OF MEDICINE, Rome and Salerno, Italy, Sept. 13-20, 1954. For information write: Segreteria XIV Congresso Internazionale di Storia della Medicina, Instituto di Storia della Medicine, Citta Universitaria, Rome, Italy.

INTERNATIONAL CONGRESS OF HYDATID DISEASE, Madrid, Spain, Sept. 25-30, 1954. Dr. Jesus Calvo Melendro, Hospital Provincial, Sorea, Spain, Secretary General.

INTERNATIONAL CONGRESS FOR INDIVIDUAL PSYCHOLOGY, Zurich Switzerland, July 26-29, 1954. For information write: Dr. E. Schmid, 14, Kronleinstrasse, Zurich, Switzerland.

INTERNATIONAL CONGRESS OF INDUSTRIAL MEDICINE, Naples, Italy, Sept. 13-19, 1954. Professor Scipione Caccuri, Director, Institute of Industrial Medicine Policlinico, Naples, Italy, Chairman, Organizing Committee.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Stockholm, Sweden, Sept. 15-18, 1954. Professor Anders Kristenson, Karolinska Sjukhuset, Stockholm 60, Sweden, Secretary-General.

INTERNATIONAL CONGRESS ON MENTAL HEALTH, University of Toronto, Toronto, Ontario, Canada, Aug. 14-21, 1954. For information write: Executive Officer, International Congress on Mental Health, 111 St. George St., Toronto, Ontario, Canada.

INTERNATIONAL CONGRESS OF NUTRITION, Amsterdam, Netherlands, Sept. 13-17, 1954. Dr. M. van Eekelen, Centraal Instituut voor Voedingsonderzoek T.N.O., 61 Catharynesingel, Utrecht, Netherlands, General Secretary.

INTERNATIONAL CONGRESS OF OPHTHALMOLOGY, University of Montreal and McGill University, Montreal, Canada, Sept. 9-11, 1954, and Waldorf-Astoria, New York, N. Y., U. S. A., Sept. 12-17, 1954. Dr. William L. Benedict, 100 First Avenue Building, Rochester, Minn., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF ORTHOPEDIC SURGERY AND TRAUMATOLOGY, Berne, Switzerland, Aug. 30-Sept. 3, 1954. For information write: Professor M. Dubois, Isle-Hospital, Berne, Switzerland.

INTERNATIONAL CONGRESS FOR PSYCHOTHERAPY, Zurich, Switzerland, July 21-24, 1954. Dr. H. K. Fierz, Theaterstrasse 12, Zurich 1, Switzerland, Secretary General.

INTERNATIONAL GERONTOLOGICAL CONGRESS, London and Oxford, England, July 12-22, 1954. Prof. R. E. Tunbridge, General Infirmary, Department of Medicine, The University, Leeds, England, President.

INTERNATIONAL HOSPITAL CONGRESS, Lucerne, Switzerland, May 30-June 3, 1955. Capt. J. E. Stone, International Hospital Federation, 10 Old Jewry, London, E.C.2, England, Hon. Secretary.

INTERNATIONAL INSTITUTE ON CHILD PSYCHIATRY, Toronto, Canada, Aug. 13-14, 1954. Miss Helen Speyer, International Association for Child Psychiatry, 1790 Broadway, New York 19, N. Y., U. S. A., Executive Officer.

INTERNATIONAL POLIOMYELITIS CONGRESS, University of Rome, Orthopedic Clinic, Rome, Italy, Sept. 6-10, 1954. Mr. Stanley E. Henwood, 120 Broadway, New York 5, N. Y., U. S. A., Executive Secretary.

INTERNATIONAL SOCIETY OF BLOOD TRANSFUSION, Paris, France, Sept. 12-19, 1954. For information write: Colonel Julliard, Société Internationale de Transfusion Sanguine, 53 Boulevard Diderot, Paris 12°, France.

INTERNATIONAL SOCIETY FOR CELL BIOLOGY, Leiden, Netherlands, Sept. 1-7, 1954. Professor Peter J. Gaillard, University of Leiden, Leiden, Netherlands, Secretary.

INTERNATIONAL SOCIETY OF GEOGRAPHICAL PATHOLOGY, Washington, D. C., U. S. A., Sept. 6-10, 1954. Professor Fred C. Roulet, Hebelstrasse 24, Basel, Switzerland, Secretary-General.

IRISH MEDICAL ASSOCIATION, Killarney, Ireland, July 7-10, 1954. Dr. P. J. Delaney, 10, Fitzwilliam Place, Dublin, Ireland, Medical Secretary.

JAPAN MEDICAL CONGRESS, Kyoto University and Kyoto Prefectural Medical College, Kyoto, Japan, April 1-5, 1955. Dr. Mitsuharu Goto, University Hospital, Medical Faculty of Kyoto University, Kyoto, Japan, Secretary General.

LATIN AMERICAN CONGRESS ON GYNECOLOGY AND OBSTETRICS, Sao Paulo, Brazil, July 10-15, 1954. Prof. Dr. Jairo Ramos, av. Brigaderio Luiz Antonio, 278-8° andar, Sao Paulo, Brazil, Chairman of Organizing Committee of Medical Congresses.

LATIN AMERICAN CONGRESS ON MENTAL HEALTH, Sao Paulo, Brazil, July 17-22. For information address: Professor A. C. Pacheco e Silva, Avenida Brigadeiro Luiz Antonio 651, Sao Paulo, Brazil.

MEDICAL WOMEN'S INTERNATIONAL ASSOCIATION CONGRESS, Lake Garda, Italy, Sept. 15-21, 1954. Dr. Ada Chree Reid, 118 Riverside Drive, New York 24, N. Y., U. S. A., President.

PAN AMERICAN CONGRESS OF GASTROENTEROLOGY, Sao Paulo, Brazil, July 19-24, 1954. For information address: Dr. Jairo Ramos, Avenida Brigadeiro Luiz Antonio 278-8° andar, Sao Paulo, Brazil.

PAN AMERICAN CONGRESS OF OPHTHALMOLOGY (Interim), Sao Paulo, Brazil, June 17-21, 1954. Dr. Moacyr E. Alvaro, Consolacao 1151, Sao Paulo, Brazil, President.

PAN AMERICAN CONGRESS OF PEDIATRICS, Sao Paulo, Brazil, Aug. 1-7, 1954. For information address: Dr. Jairo Ramos, Avenida Brigaderio Luiz Antonio 278-8° andar, Sao Paulo, Brazil.

PAN AMERICAN HOMEOPATHIC MEDICAL CONGRESS, Hotel Gloria, Rio de Janeiro, Brazil, S. A., Oct. 2-13, 1954. Dr. Paul S. Schantz, 103 West Main St., Ephrata, Pa., U. S. A., Executive Secretary.

PAN-PACIFIC SURGICAL CONGRESS, Honolulu, Hawaii, Oct. 7-18, 1954. Dr. F. J. Pinkerton, Suite 7, Young Bldg., Honolulu 13, Hawaii, Director General.

SOUTH AMERICAN CONGRESS OF ANGIOLOGY, Sao Paulo, Brazil, July 1954. For information write: Dr. Rubens Carlos Mayall, Rua Senador Vergueiro 73, Rio de Janeiro, Brazil, S. A.

WORLD CONGRESS OF CARDIOLOGY, Washington, D. C., U. S. A., Sept. 12-18, 1954. Dr. L. W. Gorham, 44 East 23d St., New York 10, N. Y., U. S. A., Secretary-General.

WORLD CONGRESS OF INTERNATIONAL SOCIETY FOR THE WELFARE OF CRIPPLES, Scheveningen-The Hague, Netherlands, Sept. 13-17, 1954. Secretariat: Miss H. P. Post, Pieter Lastmarkade 37, Amsterdam Z, Netherlands.

WORLD FEDERATION OF OCCUPATIONAL THERAPISTS, Edinburgh, Scotland, August 17, 1954.

WORLD MEDICAL ASSOCIATION, Rome, Italy, Sept. 26-Oct. 2, 1954. Dr. Louis H. Bauer, 345 East 46th St., New York 17, N. Y., U. S. A., Secretary-General.

EXAMINATIONS AND LICENSURE

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various Centers, July 16. Final date for filing applications was Jan 16. Sec., Dr. Curtiss B. Hickox, 80 Seymour St., Hartford 15.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written.* Various centers, Sept. 2. *Oral.* Ann Arbor, Oct. 15-18. To be eligible candidates must have completed thirty-six months of training by October 1. Final date for filing application was May 1. Exec. Sec., Miss Janet Newkirk, 129 E. 52nd St., New York 22.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* New York, Sept. 22-24 (candidates on the east coast). The closing date for acceptance of applications was April 1. *Written* Oct. 18. Final date for acceptance of applications was May 1. *Subspecialties. Allergy.* New York, Sept. 23 and *Pulmonary Disease.* New York, Sept. 24. Closing date for acceptance of applications was May 10. Exec. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* New Haven, November. Final date for filing application is November 1. Sec., Dr. Leonard T. Furlow, 600 S. Kingshighway, St. Louis 10.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Deadline for receipt of applications is October 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Practical examinations, 1954.* New York City, Dec. 5-9. Final date for filing applications was July 1, 1953. *Written, 1955.* Various cities, Jan. 24-25. Final date for filing application is July 1, 1954. *Practical examinations, 1955.* Philadelphia, June 10-15; Chicago, Oct. 9-14. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Final date for filing applications for Part II is Aug. 15. Sec., Dr. Harold A. Sofield, 122 South Michigan Ave., Chicago 3, Ill.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Chicago, Oct. 8-10 and New Haven, December. Ex. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION. *Oral and Written.* Washington, D. C., Sept. 5-6. Final date for filing applications was March 31. Sec., Dr. Earl C. Elkins, 30 N. Michigan Ave., Chicago.

AMERICAN BOARD OF PREVENTIVE MEDICINE: *Parts 1 and 2.* Buffalo, Oct. 9-11. Final date for filing applications is July 15. Sec., Dr. Ernest L. Stebbins, 615 N. Wolfe St., Baltimore.

AMERICAN BOARD OF PROCTOLOGY. *Parts I and II.* Philadelphia, Sept. 25-26. *Examination in Proctology and Anorectal Surgery.* Sec., Dr. Louis A. Buie, 102-110 Second Ave., Rochester, Minn. After July 1, 1954 address Dr. Stuart T. Ross, Secretary, 131 Fulton Ave., Hempstead, New York.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 13-14; New Orleans, Feb. 28-March 1, 1955; San Francisco, Mid-October, 1955; New York City, December, 1955. Sec., Dr. David A. Boyd, 102-110 Second Ave. S.W., Rochester, Minnesota.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Washington, D. C., September. Final date for filing application for the September examination was May 1. Sec., Dr. B. R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

DEATHS

Shields, George Patrick ⊕ Captain, U. S. Navy, retired, San Francisco; born in Oil City, Pa., in 1889; University of Pennsylvania School of Medicine, Philadelphia, 1914; interned at the Methodist Episcopal and St. Agnes hospitals in Philadelphia; commissioned in the Naval Reserve Force on Feb. 5, 1917, was called into active service, remaining on active duty until Nov. 1, 1948, when he retired; as a junior medical officer early in his naval career, served at various naval medical activities along the Eastern Seaboard, including tours of duty at the Naval Academy, Annapolis, Md., the Naval Home, Philadelphia, the Naval Medical School and the Naval Hospital, Washington, D. C.; in 1924 assigned to fitting out the medical division of the USS Marblehead; on the commissioning of the ship, he remained aboard her as the senior medical officer until July, 1926; in addition to this service, served with the Marine Expeditionary Force in Haiti, and was a physician assigned to the American Olympic Team for the 1920 games held at Antwerp, Belgium; served as a regimental surgeon of the Fourth Marines stationed at Shanghai, China; also, while on Asiatic duty, served as a senior medical officer of the USS Beaver; later in his naval career was frequently assigned to naval hospitals throughout the United States as head of the urologic department; during World War II served in a variety of assignments and was commanding officer of two naval hospitals in the South Pacific; returning to the United States in 1945 served as executive officer of the Naval Hospital, Chelsea; ordered to duty as commanding officer of the Naval Hospital, Parris Island, S. C., where he served until 1947, when he was ordered to San Francisco, as staff medical officer, Pacific Reserve Fleet, and was serving in this assignment until the time of his retirement; died in U. S. Naval Hospital, Oakland, April 16, aged 64, of cerebral hemorrhage and arteriosclerosis.

Mosenthal, Herman Otto ⊕ New York City; born in New York July 8, 1878; Columbia University College of Physicians and Surgeons, New York, 1903; assistant instructor in medicine and associate and instructor in biological chemistry at Columbia University from 1908 to 1914; associate professor of medicine and associate physician, Johns Hopkins University School of Medicine and Hospital in Baltimore from 1914 to 1918; associate clinical professor of medicine, New York Medical College, Flower and Fifth Avenue Hospitals; served on the faculty of the New York Post Graduate Medical School and Hospital, Columbia University; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; an Associate Fellow of the American Medical Association; member of the Association of American Physicians, New York Academy of Medicine, International Society of Gastroenterology, American Society of Advancement of Clinical Investigation, Society of Experimental Biology and Medicine, American Society for Clinical Investigation, and Nu Sigma Nu; in 1935 chairman of the New York Diabetes Association and member of its board of directors since 1936; president of the American Diabetes Association, 1941-1942, when he became a member of the council; captain, Medical Officers Reserve Corps, 1918-1919; attending physician in diseases of metabolism, Vanderbilt Clinic, from 1910 to 1914; assistant visiting physician, Presbyterian Hospital, from 1911 to 1914; consulting physician, Bellevue Hospital, New York City and Sea View Hospital, Staten Island; consultant, St. Luke's Hospital, Newburgh, N. Y., Goshen (N. Y.) Hospital, and New York Infirmary for Women and Children; affiliated with Doctors Hospital, where he died April 24, aged 75, of uremia due to nephrosclerosis.

Slaughter, William Howard ⊕ Medical Director, U. S. Public Health Service, retired, Richmond, Calif.; born in Tensaw, Ala., Sept. 2, 1886; University of Virginia Department of Medicine, Charlottesville, 1912; interned at Waltham (Mass.) Hospital and the Contagious Disease Hospital (now the U. S. Marine Hospital), Ellis Island, N. Y.; commissioned an assistant surgeon in the U. S. Public Health Service in 1913; promoted to passed assistant surgeon in 1918, surgeon, 1921, senior surgeon, 1933, and medical director in 1939; retired in 1940; during World War I in charge of the Extra-Cantonement Zone at Fort Sill and Camp Doniphan, Okla.; relieved from this duty to assume charge of the Extra-Cantonement Zone at Fort Moultrie, and the Navy Yard, Charleston, S. C.; his duties varied, including hospital, research, immigration inspection, and sea patrol; from 1935 to 1939 professor of preventive medicine and public health at Louisiana State University School of Medicine, New Orleans; fellow of the American College of Surgeons; member of the American Public Health Association and the Association of Military Surgeons of the United States; in October, 1935, delivered the Chaille memorial oration before the Orleans Parish Medical Society; served at U. S. Marine hospitals in Mobile, Ala., Cleveland, Memphis, Tenn., Galveston, Texas, New Orleans, and Chicago; made several contributions to medical literature; died in the U. S. Public Health Service Hospital in San Francisco April 28, aged 67, of multiple myeloma.

Singer, Jacob Jesse ⊕ Beverly Hills, Calif.; born in Leeds, England, July 12, 1882; Washington University School of Medicine, St. Louis, 1904; associate clinical professor of medicine at the University of Southern California School of Medicine in Los Angeles from 1938 to 1944; served as associate professor of clinical medicine at his alma mater in St. Louis, where he was consultant in diseases of the chest at Barnes Hospital, Jewish Hospital, Children's Hospital, and U. S. Marine Hospital for many years; at one time affiliated with the U. S. Public Health Service; an Associate Fellow of the American Medical Association; fellow of the American College of Physicians; member of the American Association of Thoracic Surgery, Central Society for Clinical Research, American College of Chest Physicians, and the American Trudeau Society; specialist certified by the American Board of Internal Medicine; consultant in diseases of the chest, Los Angeles Sanatorium in Duarte, where in 1942 he was appointed medical director, and Cedars of Lebanon Hospital; medical director of the Rose Lampert Graff Foundation; joint author with Drs. Evarts A. Graham and Harry C. Ballon, of "Surgical Diseases of the Chest"; author of "Differential Diagnosis of Chest Diseases"; died April 13, aged 71, of coronary thrombosis.

Bulson, Eugene Loring ⊕ Fort Wayne, Ind.; born in Fort Wayne, Ind., Feb. 26, 1894; Indiana University School of Medicine, Indianapolis, 1920; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and the Association for Research in Ophthalmology; fellow of the American College of Surgeons; past president of the Fort Wayne Academy of Physicians and Surgeons; editor of the academy's publication "The Caduceus" for many years; served during World War I; affiliated with St. Joseph Hospital, where he was president of the staff; for 25 years president of the Fort Wayne Magicians Club; died April 13, aged 60, of coronary occlusion.

Charbonnet, Pierre Numa ⊕ Pass Christian, Miss.; born in New Orleans Oct. 19, 1890; Tulane University of Louisiana School of Medicine, New Orleans, 1916; at one time on the faculty of his alma mater; member of the Oklahoma State Medical Association; specialist certified by the American Board of Obstetrics and Gynecology; served overseas in World War I and was awarded the Purple Heart; formerly practiced in Tulsa, Okla., where he was chief of staff of St. John's Hospital in 1929 and chief of the hospital's department of obstetrics and gynecology from 1927 to 1949, and affiliated with Hillcrest Hospital; died Feb. 2, aged 63, of coronary thrombosis.

Armstrong, Alfred Warren, Canandaigua, N. Y.; Syracuse University College of Medicine, 1904; fellow of the American College of Surgeons; served during World War I; consultant in surgery, for 36 years director, and for 30 years secretary of the board, Frederick Ferris Thompson Hospital, where he died March 4, aged 77, of malignant lesion of the brain.

⊕ Indicates Member of the American Medical Association.

Ault, Charles Aaron Jr. ⊕ Dallas, Texas; Baylor University College of Medicine, Dallas, 1937; served during World War II; affiliated with Baylor University Hospital and the East Dallas Hospital, where he died March 31, aged 40, of coronary occlusion.

Biltz, Robert Lincoln ⊕ Newport, Ky.; University of Cincinnati College of Medicine, 1927; county health officer; affiliated with William Booth Memorial Hospital, where he was past president of the staff, and St. Elizabeth Hospital in Covington, Speers Hospital in Dayton, and Children's Hospital in Cincinnati; died March 27, aged 52, of acute coronary occlusion.

Bonsignore, Anthony, Brooklyn; Regia Universita degli Studi di Catania. Facolta di Medicina e Chirurgia, Italy, 1905; affiliated with the Columbus Hospital in New York and the Brooklyn Doctors Hospital; died March 18, aged 75, of cerebral hemorrhage.

Booth, Bernard Hess ⊕ Drew, Miss.; Memphis (Tenn.) Hospital Medical College, 1902; served during World War I; died April 9, aged 77, of coronary thrombosis.

Broadman, Nathaniel, New York City; Eclectic Medical College, Cincinnati, 1920; died March 22, aged 75, of cerebral hemorrhage.

Bullock, Charles C. ⊕ West Chester, Pa.; Jefferson Medical College of Philadelphia, 1889; affiliated with Chester County Hospital; died April 9, aged 91, of cerebral hemorrhage.

Cabaniss, William Harvey ⊕ Athens, Ga.; University of Virginia Department of Medicine, Charlottesville, 1911; served during World War I; died in Leesburg, Fla., April 13, aged 68, of acute pulmonary edema and coronary insufficiency.

Cady, Donald Watson ⊕ Pasadena, Calif.; University and Bellevue Hospital Medical College, New York, 1921; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology and the Pacific Coast Oto-Ophthalmological Society; fellow of the American College of Surgeons; affiliated with the Huntington Memorial Hospital, where he died April 14, aged 60, of massive upper gastrointestinal hemorrhage.

Cranston, William Johnston ⊕ Walton, N. Y.; Bellevue Hospital Medical College, New York, 1894; an Associate Fellow of the American Medical Association; affiliated with Benedictine Hospital in Kingston and the Delaware Valley Hospital, where he died Feb. 28, aged 88, of uremia.

Crawford, James Harden ⊕ Atlanta, Ga.; Atlanta College of Physicians and Surgeons, 1900; affiliated with Georgia Baptist Hospital and St. Joseph's Infirmary; died April 11, aged 74, of Laennec's cirrhosis of the liver.

Crowe, Vernon Earl ⊕ Tacoma, Wash.; Bennett Medical College, Chicago, 1914; past president of the Pierce County Medical Society; died in Tacoma General Hospital April 11, aged 64, of carcinoma of the urinary bladder.

Culhane, Thomas Henry Jr. ⊕ Rockford, Ill.; Chicago Medical School, 1935; member of the Industrial Medical Association; served during World War II as a flight surgeon with the Ninth Air Force; died April 17, aged 49, of viral myocarditis.

Cullen, Archie Irving ⊕ Altamont, N. Y.; Albany (N. Y.) Medical College, 1903; health officer of the town of Guilderland since 1936; from 1937 to 1952 health officer of the town of Knox and from 1942 to 1946 was health officer of the village of Altamont; served as president of the board of education of the Altamont High School; died April 3, aged 73, of coronary thrombosis.

Cunning, I. H., Knobel, Ark.; Kentucky School of Medicine, Louisville, 1900; died in Baptist Memorial Hospital, Memphis, Tenn., April 7, aged 76, of coronary thrombosis.

Davis, Melvin Reid, Bridgeport, Conn.; Howard University College of Medicine, Washington, D. C., 1924; affiliated with Bridgeport Hospital; died April 1, aged 57, probably of acute coronary occlusion.

Duke, John W., Hindman, Ky.; Kentucky School of Medicine, Louisville, 1896; for many years county health officer; died April 16, aged 80, of a heart attack.

Errico, Louis, New Haven, Conn.; Yale University School of Medicine, New Haven, 1921; member of the International College of Surgeons; affiliated with Hospital of St. Raphael; died April 3, aged 61, of heart disease.

Feldman, Jacob B. ⊕ Philadelphia; Jefferson Medical College of Philadelphia, 1908; affiliated with Episcopal Hospital and St. Christopher's Hospital for Children; died March 27, aged 69, of acute coronary occlusion.

Froehlich, Alexander I. ⊕ McHenry, Ill.; Marquette University School of Medicine, Milwaukee, 1913; served during World War I; for many years member of the local school board; died in the Victory Memorial Hospital, Waukegan, April 17, aged 63, of acute coronary thrombosis and atherosclerosis.

Gable, Homer Benjamin, Monticello, Ind.; Chicago College of Medicine and Surgery, 1909; secretary of the White County Medical Society from 1917 to 1945; formerly county coroner; for many years city health officer, and surgeon for the Monon and Pennsylvania railroads; affiliated with St. Joseph and Memorial hospitals in Logansport; died Feb. 7, aged 68, of coronary thrombosis.

Gillespie, Joseph Franklin ⊕ Greencastle, Ind.; Bellevue Hospital Medical College, New York, 1890; an Associate Fellow of the American Medical Association; died March 16, aged 90, of uremia.

Glatzer, George Leonard, Brooklyn; Baylor University College of Medicine, Dallas, 1938; attending physician at Kings County Hospital; on the staffs of the Jewish Sanitarium and Hospital for Chronic Diseases and the Madison Park Hospital; died in the Israel Zion Division of Maimonides Hospital April 6, aged 43, of myocarditis.

Gowdy, Francis Adelbert ⊕ Fort Pierce, Fla.; the Hahnemann Medical College and Hospital, Chicago, 1896; member of the medical staff at Fort Pierce Memorial Hospital; died April 6, aged 82, of congestive heart failure, arteriosclerosis, and cerebrovascular accident.

Grover, Fred Clayton, Duluth, Minn.; Minneapolis College of Physicians and Surgeons, medical department of Hamline University, 1906; died March 9, aged 79, of cerebral sclerosis.

Hill, Clarence, Frankfort, Ind.; Medical College of Indiana, Indianapolis, 1898; died March 19, aged 79, of coronary thrombosis.

Hull, William Harry ⊕ Elyria, Ohio; Medical College of Ohio, Cincinnati, 1908; examining physician for the local Selective Service Board during World Wars I and II; on the staff of the Gates Hospital for Crippled Children and Elyria Memorial Hospital, where he died April 10, aged 69, of arteriosclerotic heart disease and cardiac insufficiency.

Kennedy, David Ross ⊕ Paducah, Ky.; Jefferson Medical College of Philadelphia, 1921; on medical staff, F. H. McGraw Hospital (AEC Plant); died March 24, aged 58, of coronary occlusion.

Killory, George Leo, Boston (licensed in Massachusetts in 1900); served on the staffs of the Massachusetts General and Boston City hospitals; died March 21, aged 75, of cerebral hemorrhage.

Kirby, Benjamin B., Dadeville, Mo.; Missouri Medical College, St. Louis, 1894; president of the school board, affiliated with St. John's and Baptist hospitals in Springfield; died in Eldorado Springs March 6, aged 87, of heart disease.

Kittredge, Patrick James, Portsmouth, N. H.; Baltimore Medical College, 1906; served during World War I; city physician for many years; died March 20, aged 77, of arteriosclerosis.

Klebba, Paul Anthony ⊕ Detroit; Detroit College of Medicine and Surgery, 1914; served overseas as a medical officer during World War I; in December, 1934, named director of the Wayne County Pathological Laboratory; became chief medical examiner in October, 1951; chief medical officer for the Detroit Service Railway; served as chief medical consultant for the Ford Motor Company; on the staff of St. Joseph Mercy Hospital; died in the Henry Ford Hospital March 24, aged 63, of myocardial infarction.

Larway, John L., Indianapolis; Eclectic Medical Institute, Cincinnati, 1898; died in St. Vincent's Hospital March 6, aged 84, of coronary occlusion.

Lesser, Robert Philipp ⊕ Oakland, Calif.; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1918; died in San Francisco Feb. 16, aged 62, of heart disease.

Lovett, Charles Earl, Lineville, Iowa; Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1907; affiliated with Decatur County Hospital in Leon; died in Weatherford, Okla., March 15, aged 70, of coronary occlusion.

Luzadder, John Edmund ⊕ Bloomington, Ind.; Kentucky School of Medicine, Louisville, 1892; affiliated with Bloomington Hospital; died March 22, aged 83, of coronary thrombosis.

Lynn, James Fristoe, Waseca, Minn.; University College of Medicine, Richmond, 1896; past president of the Waseca County Medical Society; served during World War I; for many years president of the board of health of Waseca; health officer; died March 23, aged 82, of coronary thrombosis.

Mahan, Lillian Gertrude Bullock ⊕ San Diego, Calif.; Eclectic Medical College of the City of New York, New York City, 1895; for many years physician for the school system; died in El Cajon March 27, aged 86, of chronic myocarditis.

Manley, Charles Rothwell ⊕ Santa Barbara, Calif.; University Medical College of Kansas City, Mo., 1910; member of the Washington State Medical Association; medical missionary in India for many years; died in Palm Springs March 27, aged 71, of bronchopneumonia.

Matchan, Glenn Robert ⊕ St. Louis Park, Minn.; University of Minnesota College of Homeopathic Medicine and Surgery, Minneapolis, 1899; died March 27, aged 77.

Morrison, Edward Deroy, Los Angeles; Drake University College of Medicine, Des Moines, 1901; died Feb. 21, aged 77, of osteoporosis and pulmonary embolism.

Nave, Harry E., Fountaintown, Ind.; Eclectic Medical College of Indiana, Indianapolis, 1905; died in W. S. Major Hospital, Shelbyville, March 15, aged 76, of myocardial infarction and coronary sclerosis.

Nichols, James R. ⊕ Austin, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1893; past president of the Travis County Medical Society; at one time practiced in Greenville, serving as Hunt County physician and health officer and as local surgeon for the Texas Midland Railroad; died March 2, aged 83, of coronary occlusion.

Park, Ira Oscar ⊕ Memphis, Tenn.; Vanderbilt University School of Medicine, Nashville, 1915; member of the American Academy of General Practice; died in Baptist Hospital Feb. 20, aged 62, of coronary heart disease.

Prichard, George Winthrop ⊕ Omaha; University of Nebraska College of Medicine, Omaha, 1908; died in the Immanuel Hospital March 7, aged 74, of multiple cerebral thrombosis and arteriosclerosis.

Roush, Dwight Irven ⊕ Pinellas Park, Fla.; the Hahnemann Medical College and Hospital, Chicago, 1915; affiliated with Mound Park Hospital in St. Petersburg; died March 4, aged 79, of arteriosclerosis.

Ruben, Isadore Samuel ⊕ Buffalo; University of Buffalo School of Medicine, 1920; died April 18, aged 72.

Ryan, Harry Richard ⊕ Rutland, Vt.; University of Vermont College of Medicine, Burlington, 1904; fellow of the American College of Physicians; died in Sarasota, Fla., March 19, aged 71, of myocardial infarction.

St. Clair, Harry Patton, Butler, Pa.; Ohio Medical University, Columbus, 1902; member of the medical staff at the Butler County Memorial Hospital; died March 31, aged 77, of arteriosclerotic heart disease and pulmonary edema.

Schaible, Ernst Lennox ⊕ Gary, Ind.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1908; formerly mayor; served during World War I; died in Sarasota, Fla., March 6, aged 74, of rupture of abdominal aortic aneurysm and arteriosclerosis.

Schlegman, Saul ⊕ White Plains, N. Y.; Cornell University Medical College, New York, 1909; specialist certified by the American Board of Pediatrics; on the staffs of St. Agnes and White Plains hospitals; died in April, aged 67.

Scott, George Warren ⊕ Irving, Texas; University of Arkansas School of Medicine, Little Rock, 1937; member of the Oklahoma State Medical Association; served during World War II; died April 1, aged 42, of carcinoma of the lung.

Seay, Joseph Ansa ⊕ Wichita Falls, Texas; Kentucky School of Medicine, Louisville, 1904; died recently, aged 74, of a heart attack.

Segar, H. Launcelot ⊕ Warsaw, Va.; Medical College of Virginia, Richmond, 1898; a director of the Northern Neck State Bank; died March 6, aged 84.

Smith, A. Burton ⊕ Wyoming, Pa.; Medico-Chirurgical College of Philadelphia, 1905; member of the National Gastroenterological Association; served during World War I; affiliated with Nesbitt Memorial Hospital in Kingston; died March 16, aged 84, of pulmonary edema.

Smith, James Madison ⊕ Nashville, Ind.; Indiana University School of Medicine, Indianapolis, 1908; medical adviser for the Blue Cross Plan in Brown County; formerly county health officer; served overseas during World War I; died March 16, aged 70, of glioblastoma multiforme.

Stanton, William, Machias, N. Y.; University of Buffalo School of Medicine, 1889; served during World War I; died in the Olean (N. Y.) General Hospital March 20, aged 86, of arteriosclerotic heart disease and benign prostatic hypertrophy.

Stone, William ⊕ Buffalo; University of Toronto Faculty of Medicine, Toronto, Canada, 1923; on the staff of Deaconess Hospital; died March 28, aged 56, of coronary occlusion.

Sweet, Earl Vincent, Newton, N. J.; Cornell University Medical College, New York, 1910; formerly professor of clinical medicine at Syracuse University College of Medicine; served in France with the Syracuse University Medical Unit during World War I; at one time associated with the Mutual Benefit Life Insurance Company in Newark; formerly affiliated with the Hospital of the Good Shepherd, Syracuse University; died in Hartford (Conn.) Hospital March 10, aged 75, of carcinoma.

Sweet, Edward M. ⊕ Martinsville, Ind.; Medical College of Ohio, Cincinnati, 1890; in 1906 president of the Seventh District Medical Society; for many years member of the school board, and director of the First National Bank at Martinsville; died in the Johnson County Memorial Hospital, Franklin, March 7, aged 89, of cholecystitis.

Szalony, Chester Richard, Chicago; Indiana University School of Medicine, Indianapolis, 1953; intern, St. Luke's Hospital; killed in an automobile accident March 14, aged 25.

Thomas, Eugene Marvin ⊕ Prattville, Ala.; College of Physicians and Surgeons, Baltimore, 1907; official physician for the local draft board during World War I; died in Prattville General Hospital March 15, aged 75, of cerebral hemorrhage.

Valentine, Thomas Henry ⊕ Lawrenceville, Va.; University College of Medicine, Richmond, 1901; district health officer of Brunswick-Greensville-Mecklenburg counties; died April 3, aged 75.

Wade, Arthur C., Augusta, Ga.; University of Georgia Medical Department, Augusta, 1899; died March 28, aged 78, of acute heart failure.

Wallace, Thomas Cushing Jr., Pittsburgh; Cleveland University of Medicine and Surgery, 1896; died March 22, aged 84, of coronary thrombosis.

Wilbur, Clifford Henry ⊕ Polo, Mo.; University of Kansas School of Medicine, Kansas City, Kan., 1923; served during World War I; died March 31, aged 62, of coronary occlusion.

Willoughby, Frederick Charles, Howard, S. D.; Lincoln (Neb.) Medical College of Cotner University, 1908; county health officer; died in the Sioux Valley Hospital in Sioux Falls Feb. 18, aged 77, of carcinoma of the lung.

GOVERNMENT SERVICES

AIR FORCE

General Ogle Appointed Surgeon General.—Major Gen. Dan C. Ogle has been named Surgeon General of the U. S. Air Force. He succeeds Major Gen. Harry G. Armstrong, who has been appointed Surgeon for the U. S. Air Force in Europe with headquarters in Wiesbaden, Germany. General Ogle was appointed a first lieutenant in the Medical Corps Reserve and assigned to medical duty at William Beaumont General Hospital at El Paso, Texas. Entering the School of Aviation Medicine at Brooks Field, Texas, in April, 1931, he was graduated that July; he entered the Army Medical School at Washington, D. C., three months later. He was graduated from the Medical Field Service School at Carlisle Barracks, Pa.

Major Gen. Dan C. Ogle, Surgeon General of the U. S. Air Force.

He was assigned to Chanute Field, Ill., as flight surgeon, and was named post surgeon in May, 1936. The following November he went to Luke Field, Hawaii, where he served as post surgeon. In June, 1941, he resumed his position as post surgeon at Chanute.

In 1942 General Ogle was named post surgeon of the Technical Training Center. The following March he assumed command of the Army Air Force Regional Station Hospital at Coral Gables, Fla. He went overseas in 1944 and was appointed staff surgeon of the 15th Air Force in Italy. He entered the Air War College in 1948 and was graduated in 1949. In July, 1949, he was transferred from the Army to the Air Force. The following December he was named Deputy Surgeon General of the Air Force. In March, 1953, he was named Surgeon for the United States Air Force in Europe. He has been awarded the Bronze Star medal and is rated a Flight Surgeon and Aircraft Observer (Medical).

ARMY

Short Courses for Medical Officers.—A series of short postgraduate courses for medical officers will be conducted by the Army beginning July 1, the Surgeon General has announced. The courses, designed to keep medical officers in outlying installations abreast of medical advances and to keep the health of Army personnel at a high level, are offered to both active and inactive duty medical officers as well as to physicians from other governmental agencies and civilian physicians. The courses are also open to medical officers of the Navy and Air Force. The courses will be offered on two qualification levels. Level 1 includes board-certified or board-qualified officers, chiefs or assistant chiefs of hospital services, or medical officers well advanced in the study of their specialty. In level 2 are officers partially qualified in a specialty and ward officers or dispensary surgeons responsible for medical treatment in a specialty.

The courses will be conducted at Walter Reed Army Medical Center and the Armed Forces Institute of Pathology, Washington, D. C., at Fitzsimons Army Hospital, Denver, at Letterman Army Hospital, San Francisco, and at Brooke Army Hospital, Fort Sam Houston, San Antonio, Texas.

Active duty Army medical officers and civil service physicians should submit applications to the Surgeon General, Department of the Army; reserve officers should submit applications to the army area commander where they are assigned. National Guard medical officers should make application through the National Guard Bureau, Washington 25, D. C., and medical officers from other services should apply through normal command channels. Physicians from other federal agencies and civilian physicians should apply directly to the commander of the installation offering the course.

Collaboration on Japanese Textbook.—The Armed Forces Institute of Pathology will collaborate with a group of Japanese Pathologists headed by Dr. Toru Miyaji, professor of pathology at the Osaka University medical school, in preparing a Japanese textbook on histopathology, the Surgeon General has announced. The institute will contribute about 300 photomicrographs illustrative of typical pathological states of various diseases.

Lieut. Col. Clara Raven, the U. S. Army's highest ranking woman physician on active duty, will select the illustrative material to be used in the book and will write the legends for the prints as well as a part of the text.

Dr. Miyaji recently spent three years on a fellowship at the University of Chicago and at the National Institutes of Health in Bethesda, Md. Colonel Raven, now on duty at the Armed Forces Institute of Pathology, was associated with the National Japanese Pathological Society and Japanese pathologists during her tour of duty in the Far East, 1951 to 1953. The textbook is to be published for use by Japanese medical students. Cooperation from the United States was requested for illustrations because of the difficulty of obtaining such material in the Far East.

NAVY

Retirement Credits for Attending A. M. A. Meeting.—The Chief of Naval Personnel has approved the awarding of retirement point credits to Naval Reserve medical department personnel attending the sessions of the Section on Military Medicine during the Annual Meeting of the American Medical Association, June 23 to 25, 1954, in San Francisco. One retirement point credit will be authorized for each of the three sessions attended, provided the duration of each session is at least two hours and the personnel concerned are not on the inactive status list. Not more than one retirement point will be credited for any one day. Naval district commandants have been authorized to issue appropriate duty orders without pay for attendance at this meeting.

American Leprosy Foundation.—Dr. Howard T. Karsner, Medical Research Advisor to the Surgeon General of the Navy, has been reelected chairman for another one year term of the Advisory Medical Board of the Leonard Wood Memorial (the American Leprosy Foundation). The advisory board meets annually to draft guide lines for the foundation's research, which is aimed at the cure and rehabilitation of leprosy patients. The research work toward this end is now being carried out in three centers in the Philippine Islands; in the department of microbiology, Harvard Medical School; in epidemiological studies in Texas; and in studies of the treatment of the disease in South Africa, the Philippines, and Japan. The Navy has on loan to the foundation Lieut. Jack W. Millar, M.C., for one year. Lieutenant Millar was the medical officer in charge of the leprosarium on Tinian, Mariana Islands, from its commissioning date until May 31, 1950.

Personal.—Rear Adm. Bartholomew W. Hogan, M.C., Deputy Surgeon General, was awarded the honorary degree of Doctor of Laws (honoris causa) by Villanova University in Pennsylvania on June 7, at which time he addressed a class of about 500 young men who earned degrees and 80 Villanova midshipmen who will receive commissions as ensigns in the Navy. Capt. Oliver A. Smith, M.C., Commanding Officer, Navy Dispensary, Washington, D. C., was awarded the honorary degree of Doctor of Science by Evansville College in Indiana, June 5, at the special centennial convocation.

PUBLIC HEALTH SERVICE

Life Span Goes up Nearly Four Years.—Average length of life in the United States has reached a record high of 68.5 years, a gain of nearly 4 years in the past decade, according to vital statistics compiled by the Public Health Service. The figures are based on death rates prevailing in 1951. Women on the average live longer, outliving men by six years. The average lifetime expected for women at birth is 71.8 years, while the average for men is 65.9 years. This difference in the life expectancies of men and women has increased sharply since 1900, when women outlived men by an average of only two years.

White women at birth have a life expectancy of 72.6 years, compared to 66.6 years for white men. Nonwhite groups have a shorter average life—59.4 years for nonwhite men, and 63.7 years for nonwhite women. Although white persons outlive nonwhites by an average of 8 years, the difference between the two groups has narrowed since 1900, when white persons lived about 15 years longer than nonwhites. The average length of life in 1951 generally showed little change from 1950. The 1951 figures are subject to small adjustments when detailed life tables for the years 1949-1951 become available.

Personal.—Dr. John A. Trautman has been appointed medical officer in charge of the Public Health Service Hospital at Fort Worth, Texas, and Dr. Donald W. Patrick will succeed him as director of the Clinical Center at the National Institutes of Health in Bethesda, Md., Dr. Leonard A. Scheele has announced. Dr. Trautman left his Bethesda post on June 16 to assume charge of the 1,000-bed Fort Worth institution, which is devoted mainly to treatment and study of psychiatric disorders and narcotics addiction. He has been in charge of the Clinical Center since 1951. It was under his direction that the patient care staff of the new research facility at Bethesda was assembled and the first study patients admitted in July, 1953. Dr. Patrick has been Medical Officer in Charge of the Public Health Service Hospital in Baltimore since 1949 and before that headed the Service's Hospital in Detroit, Michigan.——Dr. Robert W. Berliner has been appointed associate director in charge of research at the National Heart Institute of the Public Health Service, succeeding Dr. James A. Shannon, now associate director of the National Institutes of Health, of which the Heart Institute is a unit. Dr. Berliner was formerly chief of the Heart Institute Laboratory of Kidney and Electrolyte Metabolism. He was first appointed to the Heart Institute in 1950, after extensive research experience as leader of a group of investigators at Columbia University, New York. He also served as assistant professor of medicine at Columbia.

VETERANS ADMINISTRATION

Residencies in Psychiatry.—The Veterans Administration Hospital, Hines, Ill., still has openings for resident physicians in psychiatry beginning July 1, 1954, and Jan. 1, 1955. The hospital is a large training center accredited for training in 18 specialties of medicine. It is within easy commuting distance of the various psychiatric facilities in Chicago. The Dean's Committee is comprised of men from the four local medical schools. The training program is well rounded and accredited for full training.

Openings for Psychiatrists.—The Veterans Administration has announced that it has openings for psychiatrists who prefer to work with outpatients or who are interested in organizing or administering mental hygiene clinics. In addition, the VA needs chiefs for clinics in Cincinnati; Huntington, W. Va.; Louisville, Ky.; Wilkes-Barre, Pa.; Columbus, Ohio; Little Rock, Ark.; Wichita, Kan.; and Des Moines, Iowa.

New Hospital Managers.—Dr. Paul R. Copeland, chief medical officer of the VA center at Martinsburg, W. Va., has been named manager of the 200-bed general, medical, and surgical hospital at Beckley, W. Va., succeeding Dr. Blanton E. Russell, who recently was named manager of the new VA hospital, at Cincinnati.

Dr. Murl J. Robertson, acting manager and chief of professional services at Miles City, Mont., has been named manager of the 100-bed general, medical, and surgical hospital at Miles City, succeeding Mr. C. T. Jackson, who recently was appointed manager of the VA domiciliary at Clinton, Iowa.

Mr. John I. Spreckelmyer, manager of the VA center at Bath, N. Y., has been named manager of the 3,445-bed center at Dayton, Ohio, succeeding Mr. B. C. Moore, recently retired.

Dr. Thomas J. Hardgrove, manager of the VA hospital at American Lake, Wash., has been named manager of the new 1,000-bed neuropsychiatric hospital now under construction, at Sepulveda (Los Angeles County), Calif.

Dr. Clifford C. Woods of the Veterans Administration central office, Washington, D. C., has been named manager of the VA hospital at Omaha, succeeding Dr. John J. Tyson, who was appointed manager of the VA hospital at Durham, N. C.

Dr. John J. Tyson, manager of the VA Hospital at Omaha has been named manager of the 483-bed general, medical, and surgical VA Hospital at Durham, N. C., succeeding Dr. Horace B. Cupp, who is now area medical director, VA Atlanta office.

Hospital News.—Dr. David J. Impastato, assistant clinical professor of psychiatry, State University of New York Medical College at New York, addressed the staff of the VA hospital at Northport, L. I., March 4, on "Newer Concepts in the Practice of Electroshock Therapy."——Dr. Paul H. Hoch of the New York State Psychiatric Institute addressed the staff of the VA hospital at Northport, L. I., N. Y., March 23, on "Experimentally Produced Abnormal Mental States."

Personal.—Rear Adm. Bartholomew W. Hogan, M.C., on April 30 was assigned duty as the Deputy and Assistant Chief of the Bureau of Medicine and Surgery. Admiral Hogan succeeds Rear Adm. Clarence J. Brown, M.C., who was placed on the retired list May 1, 1954, as Vice Admiral.

MISCELLANEOUS

Symposium on Antibiotics.—The Second Annual Symposium on Antibiotics, sponsored by the division of antibiotics, Department of Health, Education, and Welfare and the journal *Antibiotics and Chemotherapy*, will be held on Oct. 20, 21, and 22, 1954, in the auditorium of the department, 4th St. and Independence Ave., S. W., Washington, D. C. The titles of contributed papers along with an abstract in triplicate of no more than 200 words must be submitted no later than Sept. 1, 1954. Titles and abstracts submitted must be approved by the program committee before being included in the program; acceptance is dependent on the suitability of the papers.

The original manuscript copies of the papers must be submitted on the day of presentation at the symposium, and they must be given to the chairman of the symposium immediately after they have been delivered. Once a manuscript has been turned over to the chairman, no alterations can be accepted. Manuscripts should be typewritten (double spaced) on one side of 8½ in. by 11 in. paper. A duplicate copy should be submitted at the same time. Glossy photographs, no larger than the manuscript paper, of all illustrations should accompany the copies of the manuscript. Prints should be sufficiently clear to permit the making of engraver's cuts without retouching and to allow reduction to about one-third size.

All manuscripts will be published in English in book form under the title "Antibiotics Annual 1954-55." In addition to contributed papers several outstanding investigators and clinicians will be invited to speak on topics related to their respective specialties. Papers are to be submitted to Dr. Henry Welch, Director, Division of Antibiotics, U. S. Department of Health, Education, and Welfare, Washington 25, D. C.

FOREIGN LETTERS

BRAZIL

Lumbar Sympathectomy.—At a meeting of the Associação Paulista de Medicina, Drs. Edmundo Vasconcellos and Faud Al Assal reported 72 extraperitoneal lumbar sympathectomies, of which 10 were bilateral. All were performed by a new technique devised by the authors. A rectilinear incision of the skin and the subcutaneous cellular tissue from the extremity of the 12th rib to a point two fingerbreadths inside the anterior superior iliac spine is made. The perimysium and a small part of the obliquus internus abdominis muscle are incised close to the costal arch. Divulsion of the transversus abdominis muscle and the fascia transversalis is accomplished. The peritoneum is dissected with a dull probe to expose the psoas minor muscle and its arcades of insertion on the anterior aspect of the lumbar spine. The peritoneum is loosened upward, and the kidney and the ureter are moved to the side to expose the diaphragmatic pillar. The inferior vena cava is dissected and moved to the side to expose the sympathetic chain. The aorta is found to the left, partially covering the sympathetic chain in a region with many lymphatic glands that may be confused with the sympathetic ganglions.

The lumbar veins are, in general, more voluminous and more numerous on the right side where they may cause difficulties, principally when they bleed. Being fragile they cannot be ligated and hemostasis is accomplished only by the use of clips or tamponade. The sympathetic chain can be identified easily by inspecting the anterolateral aspect of the lumbar spine near the insertion of the psoas muscle. In some patients, however, the sympathetic nerve is covered by a thick aponeurotic sheet, in which case careful palpation is needed to detect the chain. After the dissection of the two or three (rarely four) ganglions with a hook, the section of the communicating branches is made with scissors. After the removal of the sympathetic chain from the first to the fourth ganglions, i. e., from the diaphragmatic pillar to the pelvic promontory, a clip is placed on the distal end of the nerve. The exeresis of the first ganglion is performed by torsion and pulling of the sympathetic nerve with a Kocher forceps at the level of the pillar, thus removing the end of the dorsal chain where the first lumbar ganglion is sometimes located. During the dissection of the chain, the lumbar veins need special care, as they cross the anterior or the posterior surface of the nerve. The authors emphasize the facility of the proposed technique that permits the exeresis of the whole sympathetic chain in about 15 minutes. On the other hand, the simple muscular divulsion, beside speeding the operation, shortens the postoperative period and prevents the possibility of eventration.

The authors reported the use of the new technique on 62 patients, bilateral in 10, making a total of 72 extraperitoneal lumbar sympathectomies for obliterative thromboangiitis in 30, arteriosclerosis in 20, varicose ulcers in 6, postphlebitic syndromes in 4, atonic ulcer in one, and elephantiasis in one patient. The best results were obtained in patients with thromboangiitis, arteriosclerosis, varicose ulcers, and postphlebitic syndromes in that order. The operation is well tolerated by the patients. There were no deaths in this series.

Filariasis Control.—Dr. L. M. Deane of São Paulo reported (*Hospital, Rio de Janeiro,* **45:**187, 1954) the results of an experiment performed in Belem, Pará, to evaluate the influence of antimalarial house spraying with DDT on the transmission of filariasis. The experiment consisted in the comparison of the house density of Culex fatigans and of its natural infection rate with larvae of Wuchereria bancrofti in treated and untreated houses during a one year period (June, 1948, to June, 1949). A spray containing 5% DDT was applied to the inner walls of houses at the rate of 200 mg. per square meter of surface. Nineteen houses in a zone receiving antimalarial DDT spraying and 20 houses in a neighboring untreated zone were selected at random. Both zones were located in highly filarious districts of the city. Thirteen of the treated houses were sprayed only twice, and six were sprayed six times during the experiment. Weekly mosquito catches of 30 minutes were made in each house; the mosquitoes were counted, the species identified, and some of the females dissected and examined for filaria larvae from 24 to 48 hours after their capture. A total of 64,713 C. fatigans were collected, 39,761 of which were females; 11,900 of these were examined for filaria larvae.

The author concluded that DDT spraying as routinely performed in Belem to control malaria has reduced the density of C. fatigans in the treated houses, a decrease more striking for males but also evident for females. The drop was greater in houses treated six times than in those treated twice during the year. The female mosquitoes that entered treated houses had less opportunity to feed on the inhabitants. The residual effect of the sprays on C. fatigans was of rather short duration. In treated houses, C. fatigans had less opportunity to become infected and even less chance of surviving to the infective stage. By combining the lower density of C. fatigans females with their lower infection rate in the treated houses, it is concluded that the inhabitants of these houses had far less opportunity to acquire filariasis in the treated zone than in the untreated zone. Other insecticides are now known to be more deadly to C. fatigans than DDT. The development of insecticide-resistant mosquitoes must be kept in mind when the control of filariasis through house spraying is being planned.

Brow Presentation.—Drs. J. Onofre Araujo and A. Guariento of São Paulo reported 11 cases of brow presentation observed in 10,027 consecutive deliveries performed at the São Paulo State University Hospital (*Rev. brasil. ginecol.* **36:**203, 1953). The distribution of the three varieties of brow presentation observed were frontal left anterior in six cases, frontal right transverse in three cases, and frontal left transverse in two cases. The factors causing the deflection of the head are maternal, fetal, and ovarian. An important maternal cause is multiparity: out of the 11 cases, two women had been delivered twice, one four times, one five times, and one seven times. Another maternal cause is pelvic deformity, which was not present in any of the cases of the series. The excessively small and excessively large volume of the fetus is also considered an important factor of deflection. In this series the weight of the fetuses was from 2,501 to 3,000 gm. in two cases, from 3,001 to 3,500 gm. in five cases, from 3,501 to 4,000 gm. in three cases, and from 4,001 to 4,500 gm. in one case. Although the prognosis for the mother is generally bad, in this series there was no maternal fatality. There were two stillborn fetuses, one from a woman with placenta praevia in whom the heartbeat of the fetus was not audible on admission, and the other died during the surgical intervention (symphysiotomy). The corrected fetal mortality was 9.1%. The authors believe that the use of forceps should be limited to the patients in whom maternal and fetal conditions are favorable, especially when the fetal head is fully engaged. Three infants were delivered by forceps. The authors believe cesarean section, resorted to in six of these cases, is the treatment of choice in brow presentation, for the sake of both mother and fetus.

Atypical Pneumonia.—At a meeting of the Associação Paulista de Medicina, Dr. M. T. Lima Filho reported on 197,517 miniature roentgenograms taken at the Ipiranga Clinic of São Paulo; 2,198 of these (1.1%) showed signs of pneumopathy and 865 patients with pneumopathy were studied, disclosing 424 cases of atypical primary pneumonia. Although this disease occurred more or less indifferently in all months of the year, it was somewhat less frequently seen during the winter months, a period of the year in which upper respiratory tract infections are prevalent. Male patients predominated (70.7%), and 64.3% of the patients were 15 to 29 years of age. Radiological evidence of infiltration was limited to the lower third of the lungs in 87.5% of the patients. Most patients had symptoms of an influenzal process, with a dry, unproductive cough, and their disease ran a benign course.

The items in these letters are contributed by regular correspondents in the various foreign countries.

CHILE

Treatment of Tuberculosis.—Drs. Grossman and co-workers of Valparaiso reported the results of treating 90 patients with pulmonary tuberculosis with isoniazid (*Revista médica de Valparaiso,* September, 1953). The patients were divided into 2 groups; 34% (group 1) received no previous treatment with antibiotics, and the rest (group 2) received antibiotics that, however, were discontinued three months prior to the initiation of treatment with isoniazid. In most patients, the previous antibiotic treatment consisted in the administration of streptomycin and *p*-aminosalicylic acid (PAS) or streptomycin alone. In group 1 the lesions were exudative in 23%, caseous in 30%, and productive in 40% of the patients. Cavities were present in 77%. The dosage of isoniazid used in this group was 3 to 6 mg. per kilogram of body weight. No toxic reactions were observed. In 23%, streptomycin was added to isoniazid in doses of 1 gm. every three days. In this group improvement in the cough was noted by 80%, in the sputum by 83%, and in gain in weight by 83%. In spite of the fact that the disease in these patients was far advanced, only 17% of the patients had fever. This data differs radically from that obtained by other observers. The roentgenograms taken after three months of treatment revealed regression of the lesion in 66%, no variation in 30%, and progression in 4%. Cavitary lesions closed in 4.5%, decreased in 60%, and did not change in 35%. After the third month, group 1 was divided into two. One served as control and the other continued to receive isoniazid. This was done to determine whether after three months of treatment the drug was still effective. The authors observed no significant difference between the two subgroups.

Regarding group 2, the distribution by sex, age, extension of the lesion, and the presence of cavities did not differ fundamentally from that of the first group. The effect of the drug on the cough, sputum, and weight was less marked than in the first group. Roentgenograms showed regressions at the end of the third month in less than half the patients, but the treatment transformed progressive lesions into stationary lesions in 37% of the patients. A decrease in the size of the cavities was achieved in 40%. At the beginning of the treatment, 88% of the patients had positive sputum, but after three months of treatment only 40% had positive sputum. The corresponding figures for group 1 were 86% and 40%. After six months of therapy, there was an increase in the proportion of improved patients, but it was not statistically significant. The authors concluded that the results obtained with isoniazid in patients with advanced tuberculous lesions and with a poor prognosis are better than with any other type of chemotherapy.

Treatment of Herpes Zoster with Cortisone.—Dr. Gelfand's article on the treatment of herpes zoster with cortisone (*J. A. M. A.* **154:**911 [March 13] 1954) states that "Although steroid therapy has been used in the ocular complications following herpes zoster ophthalmicus, there has been no report concerning the effect of cortisone on herpes zoster, hence this preliminary report." Drs. M. Weinstein and R. Lamas call attention to the fact that, in the University of Chile, this type of treatment was begun in 1951 and the first results in 12 patients were reported in the *Revista médica de Chile* (**80:**266, 1952). An abstract of this work was published in THE JOURNAL (**150:**1641 [Dec. 20] 1952). Since 1951, 46 patients have been treated here; 25 with corticotropin (ACTH) in slow phlebocylsis, 18 with cortisone, and 3 with slowly absorbed corticotropin given intramuscularly. Five patients with postzonal neuralgia of more than 20 days' duration were given steroid therapy without any positive results. Herpes zoster is very sensitive to corticotropin and cortisone, and smaller amounts of these drugs than are used for any other pathological condition give good results.

The best therapeutic results, however, are obtained with intravenous instillation of corticotropin in daily doses of 0.5 to 1 mg. dissolved in one liter of 47% dextrose solution and given over a period of eight hours. This treatment cures herpes zoster in four to six days. After 15 to 20 minutes of this treatment, the patients get appreciable relief from pain. On the following day, the vesicles are more flaccid and all cutaneous manifestations disappear after one week. Regarding cortisone, 25 mg. given three or four times a day is sufficient to produce good results. In only 3 of the 46 patients did the therapy fail. None of the remaining 43 patients had neuralgia, but the authors suggest that in order to eliminate all possibility of failure it might be advisable to supplement this form of therapy with some of the antibiotics that are used currently in the treatment of herpes zoster.

Prognostic Value of the Spinal Fluid in Tuberculous Meningitis.—Drs. Howard and Aspillaga, writing in the *Revista chilena de pediatria,* state that since 1947 in the children's hospital, Luis Calva Mackenna, tuberculous meningitis has received special attention. In a previous work (*Revista chil. ped.* **23:**201, 1952) 107 such patients were treated with streptomycin given intramuscularly and intrathecally. The apparent lack of correlation between the spinal fluid findings and the clinical response to treatment motivated the present study. The spinal fluid was studied prior to the beginning of treatment and the study was repeated every 15 days for 3 months, then once a month for one year. The 93 patients examined were divided into two groups; group 1 included the 57 patients who died during the period of observation and group 2 the 36 who survived.

The albumin level was much higher in the first group than in the survivors. In both groups there was a frank decrease after the fourth month. After the sixth month among the survivors the albumin level was less than 0.5 gm. per 100 cc. and it decreased slowly toward the end of a year. The first group had a lower chloride level, but both groups showed an increase toward the end of the fourth month, the increase was much more marked in the survivors, reaching its maximum toward the seventh month and then maintaining its level. As with chlorides, the first group had lower dextrose levels than the survivors. The greatest increase in dextrose level in the first group was toward the second week and in the survivors toward the ninth month. In the first group the leukocyte counts were higher than those of the survivors. The decrease was nearly parallel in both groups until after 2½ months of therapy, then the two curves separated and the counts in the survivors continued to decrease, while in the others it was stationary or increased. No conclusion could be made from a study of the lymphocytes. The authors concluded that no single test was of prognostic value in an individual patient, but a practically normal fluid is a better prognostic sign than a fluid that is greatly altered. Even such a general statement, however, does not always hold. The authors observed several patients who recovered in spite of a greatly altered spinal fluid. The spinal fluid findings returned to normal within a year. Changes in albumin level and the cellular elements returned to normal more slowly than the other factors studied.

DENMARK

Causes of Death Among Diabetics.—Diabetes research in Denmark has been greatly facilitated by the establishment of a card index of diabetics kept by the Association of Apothecaries in connection with the rationing of sugar substitutes. In 1953, the public health authorities cooperated with the National Diabetes Association in a statistical study of this card index with reference to the occurrence and distribution of diabetes mellitus during the period 1944 to 1948. This study has now been extended to an investigation of the causes of death among diabetics, and in *Ugeskrift for laeger,* Feb. 18, 1954, Dr. Karen Dreyer and Dr. Alfred Hey presented a summary of their findings. They show that the diabetic male dies younger than the diabetic female and that diabetics of both sexes die younger than normal persons in the community. In such a study, it is difficult in many cases to decide the exact part played by diabetes itself as the principal cause of death. This Danish study shows that the combination of diabetes with cancer was much the same as that found by Joslin, 9.7% of the deaths among diabetics being due to cancer in the Danish study, while this was the case in 8.8% in Joslin's study. One of the Danish tables lists the contributions made by renal disease, arteriosclerosis, diseases of the respiratory system, heart disease, and tuberculosis to deaths among diabetics.

ENGLAND

Sport and Longevity.—A comparison of the longevity of Cambridge sportsmen and scholars attending the university between 1860 and 1890 was made by Sir Alan Rook (*Brit. M. J.* 1:773, 1954). There were 772 sportsmen including athletes, 187 cricketers, 178 rowing men, and 217 rugby players. The control group was made up of 374 "intellectuals" (honors men) and 336 "randoms" (men "who had not distinguished themselves sufficiently either academically or as sportsmen to be included in the other group"). The results show that the average age at death varied comparatively little; sportsmen died at 67.97 years, intellectuals at 69.41, and randoms at 67.43. Survival rates showed that up to the age of 40 the sportsmen had slightly better prospects, and it is suggested that this advantage is the result of deaths of weaklings in the other groups who from their physical attributes would be unlikely to indulge in sport. After 40 the sportsmen and randoms keep closely together, with the intellectuals maintaining a slight but definite lead at each age. No difference of statistical significance was found in the survival rates in the different types of sportsmen; the average age at death was 67.41 years for athletes, 68.13 years for cricketers, 67.08 years for rowers, 68.84 years for rugby players, and 67.43 years for the random group. There was some evidence that the prospect of longevity for the heavily built men was not so good as it was for the lightly built. The trend appeared to be for the heavy men to have a slight advantage over the light ones up to middle age, a tendency that is reversed with advancing years.

No evidence was found to indicate that cardiovascular causes of death were more prominent among sportsmen. Thus, among the cases in which the cause of death was known, the percentage of deaths due to cardiovascular conditions was 36.4 for athletes, 31.5 for rowers, 37.2 for cricketers, 42 for rugby players, 39.9 for intellectuals, and 41.5 for randoms. In the control (random) group, 27.3% of deaths due to cardiovascular conditions occurred before the age of 65, compared with 22.5% in the sportsmen. Other interesting comparisons are that 97.9 per 1,000 of the sportsmen died from accident or war injuries, compared with 70.4 per 1,000 of the random group and 46.7 per 1,000 of the intellectual group. The suicide rate was 40.9 per 1,000 for the intellectuals and 8.6 per 1,000 for the remainder, a ratio of nearly 5:1. "The likelihood that these figures are due to chance are less than one in a hundred."

Conjoined Twins.—Prof. Ian Aird reported an operation that he recently performed in Hammersmith Hospital for the separation of conjoined twins (*Brit. M. J.* 1:831, 1954) born in Kano, Nigeria, to an Ibo mother on July 25, 1953. At birth, one twin presented as a vertex and the other as a breech. They were successfully delivered by a midwife. Their total birth weight was 7 lb. 13 oz. (3.5 kg.). They were breast fed by the mother. On admission to Hammersmith Hospital on Nov. 13, 1953, they weighed 19 lb. 1 oz. (8.7 kg.). One (W.) was larger and more active than the other (T.) and the facial appearance of each was quite distinct. The twins were joined by a bridge, 14 cm. in its long vertical diameter and 37 cm. in circumference, that extended from the sixth costal cartilage to the navel. There was a common navel with an umbilical hernia that could be invaginated, that admitted two fingers, and that was surrounded by a firm ring of muscle. The invaginating finger passed easily into both peritoneal cavities. In its uppermost part, the bridge contained "a hard tissue which was deduced to be cartilage . . . formed by the fusion of the sixth, seventh and eighth costal cartilages, and the lower part of the sternum." A heart beat could be heard over the chest of each child, and the twins breathed in unison and sucked synchronously when fed.

Special investigations showed the heart shadows to be clearly separate from each other. The intestines filled the lower part of the bridge, but radiologically no hollow viscera could be seen in the upper third of the bridge. In the "uppermost part of the bridge a clear gap was observed between the two livers and the outlines of the opposing faces of the two livers were thought to be distinguishable; yet there remained a rather hazy shadow between these two outlines, and a bridge of liver tissue crossing from one infant to the other could not be excluded." Examinations carried out after the feeding of an opaque meal showed stomach, intestine, colon, and rectum to be separate in each child. As the two pyloruses were at least 3 in. (7.6 cm.) apart, it was assumed that the two duodenums were separate from each other and that at least the lower ends of the common ducts were separate too. Both gallbladders were visible and well separated from each other on cholecystography. Intravenous pyelography showed the kidneys and bladders to be normally situated and separate. A study of the circulatory connections between the two infants by means of radioisotopes yielded a report stating that "41 ml. per minute of blood crossed the bridge in each direction. . . . perhaps 5 to 10 ml. per minute might cross in the skin and muscle of the bridge. There was thus 30 to 35 ml. per minute to account for by a cross-circulation in some tissue other than skin and muscle. Assuming the liver circulation to be one-third of the total circulation it might be taken that 100 ml. per minute passed to each liver," or to each half of a shared hepatic bridge. For 30 to 35 ml. to cross the bridge in each direction by way of the liver would mean that there was substantial mixing in the central 60 to 70% of a shared hepatic bridge. "The presumption that liver lay in the bridge was thus extremely strong."

Two surgical teams, each consisting of surgeon, assistant, and instrument nurses, participated in the operation, the two surgeons separating the twins and then each conducting one closure. The infants were separately intubated and anesthetized by means of a separate anesthetic apparatus, with nitrous oxide and oxygen, and without any difficulty. The initial incision was made from the cartilage bridge to the navel. "The skin having been divided, a reasonably thick sheet of abdominal muscle presented, equal to the whole thickness of the normal infantile abdominal wall, though not separated in layers. When this was divided, peritoneum appeared in the lower part of the wound" and the hepatic bridge could be detected in the upper part. Division of the liver by means of a liver tourniquet of fine soft rubber and Schumacher intestinal clamps proved less hazardous than was expected. The final suturing of the raw surfaces was facilitated by the fact that "the liver tissue proved to be so flexible and elastic that the cut edge of Glisson's capsule on the far side of the raw surface could be brought quite readily forwards for suture." The elapsed time from the first incision to the insertion of the last stitch in the second baby was 95 minutes. At the end of the operation "the babies were in as good shape as any babies of that age are after an abdominal operation."

The infants were returned to the ward in oxygen tents but, one hour later, T. suddenly died. At necropsy the adrenals were found to be about one-third of their normal weight, and it is suggested that before separation the other twin had supplied the greater part of the cortisone necessary for both. Neither twin had received cortisone postoperatively. The surviving baby gave no cause for anxiety. By the 10th postoperative day, the wound was healed, but there "remained a weakness of the lower end of the wound, and this baby has the umbilical hernia which is exceeding common among Nigerian babies." Roentgenograms showed "dextro-rotation of the heart. But the electrocardiogram is not that of a situs inversus." The mother and child left the hospital to return to Nigeria 18 days after the operation.

Antibiotics in Dermatology.—A report has just been published of the results obtained in an investigation, carried out under the aegis of the Medical Research Council, into the effect of chlortetracycline (Aureomycin), chloramphenicol, and oxytetracycline in certain dermatoses (*Brit. M. J.* 1:856, 1954). The trial was carried out on outpatients at St. John's Hospital for Diseases of the Skin, London. The dosage of each antibiotic was 2 gm. daily, divided in four doses, for three weeks unless the patient was compelled to stop because of side-effects. The treatment, in all patients who did not complete three weeks' treatment, was regarded as a failure. A compound vitamin B tablet was taken with each antibiotic capsule. Control subjects were given inert capsules. The results were as follows: Herpes simplex recurrens (31 cases, including 8 controls), no effect and one relapse under active treatment; and plantar warts (30 cases, including 9 controls), no indication of any superiority over the inert capsules. Comparable results were obtained with lichen planus (19 cases, including 4 controls), pityriasis rosea (25 cases

including 6 controls), dermatitis herpetiformis (12 cases, including 2 controls), and discoid eczema (16 cases, including 3 controls). On the other hand, seven patients with seborrhoeic infective eczema of short duration all made a rapid recovery, but five of seven whose disease was of long standing were unaffected. In 29 of 147 patients, treatment had to be suspended because of side-effects. On this the report comments, "It also became apparent that the use of large doses of these antibiotics on ambulant patients may cause such unpleasant side-effects (nausea, vomiting, and gastrointestinal upset) particularly so when aureomycin is being used as to make such treatment impracticable."

Recognition of Intoxication.—In 1951, the Council of the British Medical Association appointed a special committee to "revise and bring up to date the Association's Reports on Tests for Drunkenness (1927) and The Relation of Alcohol to Road Accidents (1935)." Under the title of "The Recognition of Intoxication," the committee has prepared a revised version of the first of these reports. Defining alcoholic intoxication as "the condition produced in a person who has taken alcohol in a quantity sufficient to cause him to lose control of his faculties to such an extent that he is unable safely to execute the occupation in which he is engaged at the material time," the committee expresses the view that "people under the influence of alcohol are responsible for several thousands of road accidents every year, in spite of the fact that official records show a much smaller number. (In 1951 the official figure was 1,300)." The point is also emphasized that "a person need not be grossly incoordinated in his movements and 'drunk' in the popular sense before he can be found to have committed an offense within the words of the Road Traffic Act."

The committee has examined the value of the blood and urine alcohol levels in the assessment of the degree of intoxication. Expired air is not considered a good medium for an estimation. Blood may be difficult to collect from an uncooperative person and if a mishap occurs it may lead to medicolegal complications and possible litigation. "Urine serves the desired purpose equally well and has the advantage that samples are easy to collect. The Committee therefore recommends that, except in special circumstances, urine should be the body fluid used." Laboratory facilities for the examination of body fluids are not at present available everywhere, but it is hoped that they will be provided in due course. The committee recommends that, when a person detained on the suspicion of being intoxicated protests that he has taken little or no alcohol, he should be given the opportunity of proving this by agreeing voluntarily to allow samples of urine to be collected for estimation of its alcohol content. It is also recommended that in the postmortem examination of victims of road accidents, samples of body fluids should be taken for analysis whenever alcoholic intoxication is suspected. In British law no official figure is laid down as the one at which it legally becomes an offense to drive a motor vehicle.

Student Health in Belfast.—In his annual report for the academic year 1952-1953 of the Student Health Service of the Queen's University of Belfast, the medical officer records that, among the 530 students, 456 defects of various types were found. Almost half of these (205) were dermatological, with ocular and dental conditions accounting for 107 cases. Of the 66 ocular defects, 41 required correction with glasses. Seventeen of the defects were classified as psychological, in 14 or 3.6% of the men and 3 or 2.1% of the women. Among 530 first year students examined by mass miniature radiography, one case of active pulmonary tuberculosis and 36 of inactive tuberculosis were found. Of the 488 students tested with tuberculin, 139, or 28.5%, had negative reactions. Of these, 121 were vaccinated with BCG. No student who received BCG since its use was started in the university in 1948 has so far contracted pulmonary tuberculosis. The annual x-ray study of all undergraduates included 2,381 students; the number of active cases of pulmonary tuberculosis was 11 (0.46%), about which 9 were already known. Thus, the new active cases constituted only 0.08%, compared with 0.35% in 1951-1952, 0.46% in 1950-1951, and 0.28% in 1949-1950.

FRANCE

Mammary Cancer and Uterine Fibroids.—A study of the association of mammary cancer and uterine fibroids has been carried on by Funck-Grentano and J. De Brux. Such an association is not common. The fact that the same pathogenic factors can produce both conditions should direct attention to those factors of endocrine origin and to clinical and therapeutic applications. Experimentally, the estrogens can produce mammary cancer in mice and fibrous tumors in guinea pig and rabbit uteri. Mammary cancer is frequently encountered in a woman who has shown biological, as well as clinical, signs of hyperfolliculinism. In 1948, Rudler reported on a 35-year-old woman in whom these two conditions developed after intensive treatment with estrone (Folliculin). In men, mammary cancer has been observed after treatment with large doses of estrogens for cancer of the prostate. The efficacy of therapy with androgens in woman is further evidence of the causal part played by estrogens in mammary cancer.

For this reason Funck-Brentano and De Brux in their report at the last meeting of the National Academy of Medicine emphasized the necessity of careful examination of the breasts in women with fibroids appearing after a long period of hyperfolliculinism and of looking for fibroids in women suffering from mammary cancer. The coexistence of these two lesions necessitates a double operation. It would seem logical to remove the cancer first if this operation had no effect on the fibroid, but the surgical shock causes the liberation of epinephrine and favors the proliferation of the epitheliomatous cells in the region operated on. The authors, therefore, recommend removal of uterus, tubes, and ovaries in a first stage and the breast amputation later.

Early Diagnosis of Gastric Cancer.—At a meeting of the National Academy of Medicine, R. A. Gutmann stated that the stomach may be divided into a vertical and horizontal portion. The former, which includes the fundus and cardiac portion, is the site of primary and ulcerating cancers. A benign ulcer in this portion does not undergo malignant change. The horizontal portion includes the angle and the pylorus and is more frequently the site of cancer than of ulcer. An ulcer in this portion, on the other hand, may undergo malignant change, and the cancer, during its initial period, contrary to general opinion, grows very slowly. Serial roentgenograms of the completely filled horizontal portion should be taken with the patient lying prone. Gastroscopy is of no use in detecting early cancers. Gastric analysis in patients with such cancers is normal or oftener shows an initial hyperchlorhydria. No other laboratory test is of aid in diagnosis. Because even an exploratory operation may, early in the course, fail to reveal any abnormality, the diagnosis should be made before an operation is advised.

Lateral Roentgenograms of the Uterus.—A new method of roentgenography of the uterus during pregnancy was described by P. Guilhem, A. Poutonnier, R. Baux, and R. Gombel (*Gynécologie et obstétrique*, no. 5, 1953). Instead of visualizing the uterus by making injections into the maternal vessels through the external iliac vessels, the authors use rays that permit recognition of the soft parts, producing thus in lateral roentgenograms a thick crescentic image of the anterior or posterior surface of the uterus and indicating the insertion of the placenta. For this purpose, they use as filters a mixture of chalk and barium. The patient is first requested to take a few deep breaths so that the fetal movements may be reduced. This method is only practicable during the last months of pregnancy. The authors have used this method in the cases of hemorrhage occurring in the last months of pregnancy in order to rule out a low insertion of the placenta or an anterior or posterior placenta praevia.

Use of Cortisone in Genital Endocrinology.—At the last meeting of the French Society of Gynecology, F. Jayles and co-workers reported on the use of cortisone in endocrinology. It inhibits the adrenotropic function of the hypophysis and may stimulate its gonadotropic function. In moderate doses, it may be used as a regulator of these two hypophysial activities. Its function is particularly interesting in case of hyperandrogenism, which the authors state is not necessarily accompanied by hirsutism or virilism. Cortisone may aid in the diagnosis of the adrenal or

ovarian origin of the androgenism. Cortisone is also indicated in treating patients with luteal functional disorders accompanied by sterility and repeated early abortions, not only in patients with disorders of hypophysoadrenal origin.

Medical Census.—The total number of physicians in France is 35,446, of whom 24,846 are general practitioners. Of the specialists, 2,092 are surgeons, 879 are gynecologists-obstetricians, 1,159 are ophthalmologists, and 556 are dermatovenereologists. The general distribution of physicians is highly unequal. About 100 rural districts have no physician, and 150 such districts have only one for 5,000 inhabitants.

ITALY

Cysts of the Central Nervous System.—At a meeting of the Italian Society of Neurosurgery in December, 1953, Professor Chiasserini of Rome presented a paper on epidermoid and dermoid cysts of the central nervous system. In regard to the pathogenesis of these cysts, the inclusion of cutaneous germinal epithelium in the structures from which various segments of the central nervous system are derived is possible in the course of the development of the embryo. The evolution toward an epidermoid or a dermoid cyst depends on the thickness of the enclosed germinal epithelium or on the early formation of the invagination. In exceptional cases, trauma could be the cause of these cysts, but, generally, trauma is more important in their later growth. Epidermoid and dermoid cysts of the central nervous system are not common, although they undoubtedly occur more frequently than is believed. In comparison to other tumors of the central nervous system, their rate varies from 0.5 to about 2%. The average patient is in the second or third decade of life. These cysts are very rare in old age, but dermoid cysts are found frequently during childhood.

Professor Chiasserini did not express an opinion as to whether these cysts are true tumors, but he said that there is no doubt about their being dysembryoplastic conditions. The pearly aspect, which need not always be present, depends on the outer layer of the capsule. Usually the content consists of a semisolid or solid mass, chalky in aspect, without blood vessels, that consists of the desquamation of the innermost callous layer of the epithelial covering of the capsule. The volume depends on the developmental phase and may range from the size of a chick-pea to that of a large orange. Despite their doughy aspect, these cysts may occupy a large space, and they may exert local pressure that may even produce atrophy of adjacent bones.

Among the complications are ruptures—spontaneous or caused by trauma or puncture—and infections. The meningeal reactions that follow the penetration of the cyst's contents into the arachnoid spaces or the ventricles range in degree from mild to fatal. These reactions are attributed to the toxicity of the contents of the cyst and are severer than those caused by degenerated cysts containing fluid. Postoperative aseptic meningitis, which should be more properly called meningeal reaction, is rather frequent. Infectious complications are usually linked to the presence of dermic sinuses. These are found mostly in dermoid cysts located in the posterior cerebral fossa and in the spinal cord. Metastatic infections are rare. Later the inflammation extends to the adjoining structures and causes local or generalized reactions.

Professor Chiasserini classified these cysts into cranial and spinal forms. The former are divided into diploic extradural and intradural types. King stated that the diploic extradural forms are from four to five times less common than the intradural forms. The germinal epithelium, which is enclosed in the bone sheath, develops gradually into the diploë, atrophying and separating the tables of the skull to the destruction of one or the other layer and developing as an intracranial and exocranial swelling. The bone defect produced by the growth of the tumor has particular characteristics that make the diagnosis of the nature of this condition almost certain. The edges are thick and clear and in festoon-like arrangement. The external swelling is usually the first manifestation, but there are cysts in which this may be absent or less evident than the internal expansion that compresses the brain and may also cause distinct signs of intracranial hypertension. The symptoms may be few even when large intracranial expansions are present. In such instances, encephalograms and arteriograms may reveal findings similar to those of subdural hematomas.

Some epidermoid or dermoid cysts that originate in the petrous bone cause an isolated peripheral type of paralysis of the facial nerve with atrophy of the petrous bone, extradural expansion in the mesocranial fossa, invasion and perforation of the squamous portion of the temporal bone, and swelling of the temporal fossa. In one of Professor Chiasserini's patients, the swelling seemed to have originated in the mastoid. Surgical treatment consists of emptying the cyst and removing the capsule. To prevent possible relapses, some authors suggest resecting *en bloc* the invaded bone, the cyst, and a segment of the dura. Intradural epidermoid and dermoid cysts are the most frequent forms and may be cerebral, ventricular, or of the arachnoid spaces of the base. Several years ago, intracerebral and intraventricular epidermoid and dermoid cysts were believed to be very rare, but the increased number of surgical interventions has revealed that they are present quite often. They have been found in all parts of the cerebrum and cerebellum. They may attain a large size in the lateral ventricles and invade both of them and also the third ventricle.

The symptoms depend on the localization of the cyst. A psychic or epileptic syndrome is alleged to occur, but this now seems doubtful. These cysts of the arachnoid spaces at the base of the brain may be located above the sella turcica and exceptionally within it, or they may be found in the angle of the pons varolii and the cerebellum, or in the posterior cerebral fossa. The last-mentioned forms may represent a phase of transition with the analogous forms in the spinal cord.

Spinal epidermoid and dermoid cysts are much less frequent than the cerebral forms. About 75 cases have been reported as compared to 300 of the cerebral forms. The symptoms depend on how deep and at what level the cysts are located. They correspond to a slow and progressive syndrome of radicular, medullar, or radiculomedullary compression in young patients. Analysis of the cerebrospinal fluid will not establish a diagnosis except rarely when elements of the cyst can be demonstrated. The pathognomonic signs are dermic sinuses, evidences of radiculomedullary compression in the corresponding location, or the aspiration of matter characteristic of the cystic contents. The treatment consists of removing the cyst when possible or emptying it and removing those parts of the capsule that do not adhere too strongly to the nervous structures. A favorable prognosis depends mainly on early intervention.

Symposium on Rheumatology.—A symposium on rheumatology was held at the Institute of Medical Symptomatology of the University of Rome in February. Prof. Eric Martin of Geneva, Switzerland, reported on the early diagnosis of chronic progressive polyarthritis and its treatment. He stated that, although corticotropin and cortisone are of value, especially when given in appropriate doses, he prefers treatment with gold salts. His statement aroused great interest, because it confirmed the viewpoint of Nugent, O'Neil, and others of Canada that the best results are obtained by the use of cortisone combined with gold salts. It not only has been proved that rheumatic arthritis is better controlled when the two medicaments are given concurrently rather than in succession, but has also been proved that the toxic effects of gold therapy are less common and less marked when the hormone is given simultaneously. It is recommended that before gold therapy is instituted tests on skin, mucous membranes, urine, and blood be made to prevent untoward reactions. Gold therapy is contraindicated in patients with nephritis or hepatic lesions, during pregnancy, and in patients with polyarthritis and anemia in whom the polyarthritis is of long standing and the sedimentation rate is normal. This therapy has no effect in patients with osteoarthritis. According to those who support the combined treatment with gold salts and cortisone, dimercaprol (BAL) is useful in preventing the toxic reactions resulting from gold therapy.

Professor Lunedei of Florence reported on rheumatism associated with scarlet fever. There are, according to him, four rheumatic conditions with various possible forms of transition. They are (1) rheumatic fever or acute articular rheumatism (Bouillaud's disease); (2) primary chronic rheumatism (rheumatic arthritis); (3) dystrophic rheumatism (periarthritis, fibrositis, and others); and (4) secondary rheumatism of known or

unknown cause. He rejected the distinction of an early or late postscarlatinal rheumatism. He affirmed instead that scarlatinal rheumatism can appear in the four forms listed. He favored tonsillectomy, not because the tonsils are the "focus" of rheumatism, but because they can, through frequent infection, aggravate the course of a polyarthritic rheumatism that is already present. On the other hand, Professor Lucherini of Rome was opposed to tonsillectomy because he never observed good results from removal of the tonsils. Professor Ballabio of Milan spoke in favor of a clear-cut distinction between ankylopoietic spondylitis and rheumatic arthritis. Although he appreciated the good results obtained with the combined treatment with gold salts and cortisone, he believes that phenylbutazone is better for treatment of spondylitis.

Surgical Treatment of Epilepsy.—At the same meeting, Professors Maspes and Marossero of Turin discussed the surgical treatment of temporal lobe epilepsy. Patients with temporal lobe epilepsy not caused by tumors can be treated surgically. About 14% of all cases of epilepsy are of this type. The diagnosis of temporal lobe epilepsy is based mainly on the clinical signs during the attacks and the type of disturbances that are present in the interval between attacks. These are characteristic of this type of epilepsy because of their frequency and because of the presence of psychic abnormalities or psychosis. In some patients the radiological findings reveal atrophic cerebral lesions that are often accompanied by compensatory bone reactions. The definitive diagnostic element is the electroencephalographic examination, which should be repeated and potentiated with various means of activation such as hyperventilation, sleep, and the use of pentylenetetrazole (Metrazol).

In contrast to other forms of cortical jacksonian epilepsy, the electroencephalogram in temporal lobe epilepsy often reveals bilateral abnormalities, and this constitutes an element of great importance in the selection of the cases to be treated surgically. The decision to operate is based on the severity and number of attacks, their resistance to medical therapy, and the presence of an electroencephalographic focus in the temporal region. The operation consists of removing as much as possible of the cortex of the temporal lobe, the amygdaloid nucleus, and the hippocampal gyrus. Professors Maspes and Marossero operated on 30 patients who were selected from 1,000 epileptics. More than 50% of those operated on were cured.

NORWAY

Death from BCG Debated in Parliament.—At a meeting of the Medical Society of Bergen (*Nordisk medicin*, April 8, 1954), details were given of the death of a 24-year-old man after BCG vaccination. His sedimentation rate had been abnormally high since childhood, but no reason for this had ever been discovered. In June, 1948, he was vaccinated with BCG according to Birkhaug's technique. A standard vaccine prepared by the Norwegian BCG Laboratory was used. He became tuberculin-positive after six weeks. A year later an abscess developed in the right axilla. This was incised and drained, but a sinus persisted. In November, 1950, an abscess starting from caries of a rib yielded bacilli of the BCG type. Several abscesses and sinuses subsequently developed in the chest and abdominal walls, and in 1951 serous meningitis developed. In September, 1951, the man was admitted to the hospital. Tuberculous foci developed in the kidneys, ribs, thoracic spine, sternoclavicular joint, the region of the trochanter, pleurae, and lungs. Bacteriological examinations showed bacilli of the BCG type. A series of guinea pigs were inoculated, but none of the animals showed signs of tuberculosis or died of it. They were killed after intervals of from six weeks to nine months, and the local reactions at the site of inoculation were found to have subsided completely. The patient died in December, 1953.

The unfortunate publicity given to this death in the lay press led to a debate in the Norwegian Parliament in April, 1954. The first speaker moved that the whole problem of BCG vaccination should come under revision. Later speakers exploited the recent death in denouncing BCG vaccination. Other laymen effectively took up the cudgels on behalf of this measure. The most effective defense of it was presented by the government spokesman responsible for medical matters in Parliament, the evidence presented having been collected by the Ministry of Health. It was pointed out that, in this instance, the Norwegian State BCG Laboratory had issued the same preparation of BCG to 128 Norwegian physicians without any of them having reported serious complications. Vaccine from the same bottle used in the fatal case had been administered to five other persons without any complication. The precautions taken at the Norwegian State BCG Laboratory are even stricter than those prescribed by the World Health Organization. BCG vaccination became compulsory in Norway in 1947. In this year, there were 1,760 deaths from tuberculosis. In 1952, there were 660 deaths from this cause. BCG vaccination is not given the credit for this remarkable achievement that primarily reflects advances in the treatment of tuberculosis, but vaccination is largely given the credit for the following data. In 1947, nearly 1,000 new cases of pulmonary tuberculosis in the age group 15 to 24 years were reported. The corresponding figure for 1952 was 400. Although about 1,000,000 of Norway's 3,000,000 inhabitants have now been vaccinated with BCG and fully 50,000,000 have thus been vaccinated throughout the world, the medical literature has contained reports of only two cases in which death could definitely be traced to BCG—the Norwegian case already referred to and a Danish case reported by Meyer.

Pneumonia Statistics.—Dr. R. Myhre and Prof. H. J. Ustvedt of the Ullevaal Hospital in Oslo have analyzed the 596 cases of pneumonia treated in this hospital in the period 1948 to 1951. They stressed the futility of general figures in gauging the mortality risks of a disease such as pneumonia. Among their 596 patients, 86 died in hospital, but to label this a case fatality rate of 14% is to ignore the part played in these patients by heart disease, cancer, pulmonary tuberculosis, etc. When the patients were classified according to their age and the above-mentioned complicating diseases, it was found that the mortality risk for young and otherwise healthy persons suffering from pneumonia was almost nil under modern conditions in the hospital. There were no deaths among 60 patients between the ages of 10 and 30 years, and there were only two deaths among the 78 patients between the ages of 30 and 40 years. There were 17 deaths among all the patients under the age of 60 years, but 13 of these also had a complicating disease. In other words, there were only four patients whose death was caused by pneumonia as a primary disease. Two of these were children, aged 2 and 5 years respectively. Both of them died on the day of admission to the hospital without having been given antibiotic treatment before admission. Between the ages of 6 and 40 years there were no deaths that were not with some serious disease other than pneumonia (*The Journal of the Oslo City Hospitals*, January, 1954).

Heart Disease and Pregnancy.—Dr. Helge Laake of Oslo has carried out a follow-up study of 116 women who suffered from organic heart disease and who subsequently became pregnant one or more times. They were treated in the Rikshospital during the period 1942 to 1951. Serving as controls were 56 nulliparae who also had organic heart disease and who were treated in the same hospital in the same period. Of the patients becoming pregnant, 109 had rheumatic and 7 had congenital lesions of the heart. This study (*Acta medica scandinavica*, no. 2, 1954) shows that in only 3.5% of the 312 pregnancies in these 116 women was it necessary to interrupt the pregnancy because of signs of heart failure. By correlating the number of births with the number of years between the last confinement and the appearance of heart failure, no connection could be established between the number of confinements and the frequency of heart failure. Neither the localization of rheumatic valvular disease of the heart nor the number of attacks of rheumatic fever seemed to be of any prognostic significance. The late prognosis was not influenced by the patient's age at the time of her confinement. The study also showed that pregnancy is not necessarily contraindicated for women with congenital heart disease. These follow-up examinations showed that the late prognosis was good in women who had rheumatic lesions of the heart and who survived pregnancy. The maternal mortality can, however, probably be further reduced by a correct selection of prospective mothers.

CORRESPONDENCE

TRIBUTES TO THE PHYSICIAN IN THE BIBLE

To the Editor:—In the correspondence section of THE JOURNAL for March 13, 1954, page 937, is an interesting letter by Dr. L. Roddis, "Tributes to the Physician," containing a number of admirable historical citations. Unfortunately the author also made a passing reference to the Bible that was quite inadequate and in part erroneous. In his article, only seven lines were allotted to the scriptures: one of these quoted the familiar verse 22 of Jeremiah 8, while the other reference was wrongly ascribed to the Book of Ecclesiastes. That is one verse from the prolix commendatory but rather platitudinous chapter 37 of Ecclesiasticus praising the physician. That book should not be confused with Ecclesiastes; it belongs to the Apocrypha, which is not canonical and is not included in the Hebrew or protestant versions of the Bible, although it is printed in the vulgate. In these times when antithetical topics such as public health, the H-bomb, and germ warfare are uttered in one breath and the phrases general practitioner and research physician are bandied about by laymen and reporters, and while our eyes and ears are wearied by continual advertising of cure-alls, nostrums, and fakes on television and radio, it may be worth while to dwell on a few thoughts in the Book of Books dealing with physicians and pharmacists not merely laudatory but also constructive, emphasizing the ideals of the medical profession.

Probably the most eloquent tribute to the physician is found in Exodus 15, 26 (A. V.): "For I am the Lord that healeth thee" that more precisely translated from the original Hebrew reads, "For I am the Lord that is thy physician." This verse is universally taken by Jew and Christian not in the sense of faith-healing but on the contrary as a tribute to the ideal and exalted status of the medical profession.

In the philosophical book of Ecclesiastes (not Ecclesiasticus), there are several passages of extreme interest to the physician. I quote four of them. The first is chapter 10, verse 2: "A wise man's heart is at his right hand; but a fool's heart at his left." A. L. Williams in the Cambridge edition comments: "A paradoxical statement of the superiority of the wise over the fool. Not, of course, that the writer intended an anatomical definition, but by a paradox he expressed the thought that a wise man's purpose and intelligence are always on the side of the more important, the more vigorous, and the more successful of his efforts. The left figuratively is the reverse of the right and plainly means the less important. We employ the word sinister, literally left hand, to express what is evil and villainous." To put it in plainer words, the term heart in the Bible as well as in all other languages is employed both literally, referring to the pump of life, and figuratively to express emotions and even wishful thinking. Here we have a reference to the intimate relation of mind and body enunciated long before modern medical psychologists invented the term psychosomatic. Even more profound is verse 14 of chapter 2: "The wise man's eyes are in his head, but the fool walketh in darkness." Why should the Bible state the obvious, that the eyes are in the head? The moral taught is a profound one. The eyes are the chief organ of perception. The scientist employs his vision to observe the phenomena of nature, and these apperceptions are carried to the brain, there to be analyzed, weighed in the balance of calm judgment, resynthesized, and finally, if need be, converted into action. This is not so in the fool. He does not think; his sensations are carried by the shortest and easiest paths directly to the heart, visceral glands, and muscles. As he is a slave of his emotions, he is in darkness intellectually and falls prey to hasty, often harmful reactions. Is not this dictum an invaluable counsel to scientists in general and physicians in particular?

A third verse in Ecclesiastes is even more fascinating. In chapter 7, verse 5, we read: "Who so keepeth the commandment will know no evil thing, and the wise man's heart knoweth time and judgment (Hebrew, justice)." Here again we must remember that the word heart both in Hebrew and in all other languages is employed literally and figuratively. In this verse, it is the literal translation that is the most significant. To appreciate fully the context, however, it is necessary to explain the Hebrew idiomatic phrase "time and the judgment (or justice)." In this expression as in many others in Hebrew, the second noun is employed in an adjectival sense qualifying the preceding noun. The accurate grammatical translation is "Who so keepeth the commandment will know no evil thing, but the heart of the wise knoweth a just span of life." How very right. It is a well known fact that wise and moral men, philosophers, and religious teachers of every race, creed, and clime practicing abstemiousness and self-restraint, and leading a serene life, be they rabbis, popes, Buddist priests, or Tibetan lamas, are noted for longevity. Note that here the authorized version of the Bible, translating the word heart literally, is more accurate as compared with the revised standard translation of 1952 that renders the word heart as mind.

Perhaps the most interesting and certainly most timely dictum of Ecclesiastes is chapter 5, verses 2 to 5. The term research is becoming fashionable nowadays. Medical and chemical laboratories are emphasizing it, physicians are taking cognizance of it, drug houses are pushing it, fancy-named foundations are collecting funds to subsidize it, and hospitals are establishing it. Yet, no less an authority than Prof. Dwight J. Ingle writes in a recent issue of the *American Scientist* (April, 1954, page 92): "Many researchers live, work, and die without an appreciation of how difficult it is to prove a fact"; and the philosopher M. Arthus asserts (Philosophy of Scientific Investigation, Baltimore, Johns Hopkins Press, 1943): "Indeed it is not in the turmoil of social life, not through academic chats nor laboratory gossip that we come to see the light, that interpretations become clear, that experiments are conceived, and conclusions reached. It is through solitary, profound and sustained meditation. In order to make some progress in the experimental science one must meditate a great deal." This whole problem of research has been succinctly analyzed by Ecclesiastes in the above-mentioned passage; however, we must bear in mind the accurate denotation of three Hebrew words, which are not very clear in English translation. First is the term for fool used in this passage. The Hebrew term *kesil* refers to the fool who is the victim of his lower emotions, a slave of sordid ambitions, and an exhibitionist. The second term "to vow" denotes a dedication to a task demanding self-restraint, abstemiousness, and often sacrifice of personal aggrandizement in the pursuit of an ideal. The third term "to pay" is the most ambiguous in translation. The original root *shallem* conveys two ideas, one "to bring to completion," and the other "peace." Thus "to pay a vow" means "to bring to a peaceful completion." Now I quote that passage (Ecclesiastes, chapter 5, verses 2 to 5). (The italics are mine.)

> Be not rash with thy mouth and let not thine heart be hasty to utter anything before God; for God is in heaven and thou upon earth; therefore let thy words be few.
> For a dream cometh through a multitude of *business;* and a fool's voice is known by a multitude of words.
> When thou vowest a vow unto God, defer not to pay it; for He hath no pleasure in fools; pay that which thou hast vowed. Better is it that thou shouldest not vow, than that thou shouldest vow and not pay.

Perhaps it is appropriate to conclude with an adage of an ancient Talmudical sage Antigonos of Socho (Ethics of the Fathers, chapter 1, verse 3):

> Be not like servants that minister to the master in order to receive a reward; but be like servants that minister to a master without a thought of reward; and let the fear of Heaven be with you.

The finest tribute to the medical profession is the fact that there are so many God-fearing men and women who dedicate themselves to such a task cheerfully, unstintingly, and often at a great sacrifice, ever holding as their ideal, "For I am the Lord that healeth thee" (Exodus, chapter 15, verse 26).

DAVID I. MACHT, M.D.
Sinai Hospital of Baltimore, Inc.
Monument St. and Rutland Ave.
Baltimore 5.

LEUKEMIA AND IRRADIATION

To the Editor:—I wish to say how much I appreciate the editorial on leukemia (*J. A. M. A.* **155:**38 [May 1] 1954). There is an unfortunate misinterpretation of statements that I made in my paper (*New England J. Med.* **250:**131-139, 1954). This error was brought to my attention by a radiologist here in Boston. My original statement, that the results of radiotherapy are unsatisfactory and that irradiation may even aggravate the disease, has to do only with cases of acute leukemia and not with chronic cases. This statement was evidently taken out of context, and it should have been made clear that it had reference only to acute leukemia. It is true that we are getting away more and more from x-ray therapy, but, on the other hand, good results are frequently obtained in chronic granulocytic and chronic lymphocytic leukemia as well as in Hodgkin's disease. Many people feel, therefore, that it is still the standard method of therapy for the cases of chronic leukemia and should not be given up without further experience.

William Dameshek, M.D.
192 Beacon St., Boston.

PERFORATION OF SIGMOID COLON

To the Editor:—The report of the case of perforation of the sigmoid colon after the ingestion of a hydrophilic colloid (*J.A.M.A.* **154:**1273 [April 10] 1954) teaches a very important lesson. Never administer bulk-producing substances without first making certain that no fecal impaction is present. From the description of the symptoms as they developed, it is quite obvious that such was the case. The reverse peristalsis (severe abdominal cramps, emesis, later perforation) was due to intestinal obstruction, in turn due to fecal impaction. The patient passed "small, hard, fecal marbles." He later passed a "huge mass of stool after straining." This surely was not all the fecal material that had accumulated in the lower colon. The authors correctly state that it was "presumed that the perforation in this patient occurred as a result of a temporary obstruction to the bowel contents . . . with gradual increase in the bulk of the fecal mass because of its hydrophilic nature." Repeated alkaline enemas administered before any indication of possible perforation was in evidence might have prevented its occurrence.

Fecal accumulation in the distal colon is a common type of constipation. It should not be treated with bulk-producing substances without paying strict attention to the possibiliy of fecal impaction. It is of utmost importance to empty the lower part of the colon before instituting this regimen. It should always be preceded by a roentgenologic study of the colonic motility. If the delay is only in the distal colon, then bulk-producing substances should be ordered with caution or, better still, should be avoided, unless the patient can be under strict supervision.

Zachary Sagal, M.D.
Pacific State Hospital
P. O. Box 100
Spadra, Calif.

HAND COMMUNICATION DURING APHASIA

To the Editor:—In 1943 I was stricken by coronary thrombosis followed by cerebral embolism, which resulted in right hemiplegia and complete aphasia. I was a shut-in within a paralyzed body and a shut-out from the world outside. It was then, by using my left hand, that I devised a code of communication, 21 hand signs. It was two and one-half years later, however, before I could express myself orally and tell an artist how to make the drawings that became the "Hand Talking Chart." I should like medical colleagues who have aphasic patients to have the chart if they wish. During the last seven years, the chart has been distributed nationally and internationally by the cooperation of editors of medical publications, and I have received hundreds of favorable reports on its use. Aphasic patients can communicate their basic needs and desires, thus dispelling their fears, helping them to a speedier recovery. Readers of The Journal can have the chart, without charge, on request.

Hamilton Cameron, M.D.
601 W. 110th St.
New York 25.

CORTISONE AND GUILLAIN-BARRÉ SYNDROME

To the Editor:—The case report in The Journal May 15, 1954, page 252, by Grant and Leopold, of Guillain-Barré syndrome occurring during cortisone therapy was of extreme interest and importance. The report indicates that resumption of cortisone (100 mg. daily) and later hydrocortisone (60 mg. daily) may have been a factor in the improvement that occurred after the second week. From my own experience with two cases and from the reported experience of others, it appears that large doses (200 to 400 mg.) of cortisone are necessary to relieve paralysis and that treatment must be continued throughout the period during which symptoms would be expected to endure. Premature diminution or cessation of cortisone administration has been responsible for severe relapses. Rather than curing the Guillain-Barré syndrome, cortisone appears to keep paralysis in abeyance until the episode runs its course. For the stated reasons, it is not too surprising that the Guillain-Barré syndrome made its appearance in a patient receiving cortisone therapy for another condition, and such an occurrence should not prevent the use of cortisone in progressive cases, so often fatal in the past.

F. Keith Bradford, M.D.
6410 Fannin St.
Houston 25, Texas.

ALLERGY TO MONOSODIUM GLUTAMATE

To the Editor:—I have observed allergy to monosodium glutamate in a mother and her son; two other siblings were not involved. The symptoms resembled those due to a gallbladder disease but may result from gastrointestinal reaction. They were manifested by epigastric fulness, eructations, distention, and upper abdominal discomfort that may become quite marked. The offending agent could not be identified for many months. X-ray studies of the gallbladder and of the upper intestine were normal; yet dyspepsia, as caused by gallbladder abnormality, followed careful dieting. They would become sick within half an hour after eating meals that had been pridefully prepared at home or by relatives. Succulent roasts and steaks, spaghetti, mild sauces, nicely prepared foods, etc., eaten at fine restaurants or at parties caused distress in these allergic patients while the other guests were enjoying themselves. The symptoms disappeared when monosodium glutamate was finally recognized as the causative agent and the mother and son avoided all foods to which it was added. This compound is present in Lawry's seasoned salt, Accent, V-8, various spaghetti sauces, some canned soups, Franco-American beef gravy, etc.

Leo H. Pollock, M.D.
1310 Bryant Bldg.
Kansas City 6, Mo.

CORONARY EMBOLISM

To the Editor:—After reading the article "Coronary Embolism" by Drs. Cheng, Cahill, and Foley (*J. A. M. A.* **153:**211-213 [Sept. 19] 1953), I agree with the authors that coronary embolism is a very rare occurrence. I have found, however, that the authors, in their brief review of the literature, have made an error and that this review is incomplete. The first case of coronary embolism, in which the diagnosis was made before death and confirmed at autopsy, was described by Korczyński, professor at the University of Kraków (*Przeglad Lekarski,* 1887, nr. 1, 3, 4, and 5). The diagnosis made by Professor Korczyński was "insufficiency of the aortic semilunar valves with thrombosis of the arterial orifices on the left side resulting from endocarditis, arterial hypoplasia, exudative pleurisy on the left, and embolism of the coronary artery, probably on the left side." The diagnosis was completely confirmed at autopsy by Professor Browicz. In reviewing the literature, Professor Korczyński collected 10 cases of coronary embolism in which the diagnosis was made after death. One case of coronary artery occlusion was described by A. Hammer (*Wein. med. Wchnschr.*, 1878). In this case, the diagnosis was made before death. The cause of death, however, was not coronary embolism but occlusion of the ostium of the coronary artery in the sinus of Valsalva by the clot of blood.

Dr. med. Stanislaw Bober
Kazimierza Wielkiego 20
Warsaw 21, Okęcie, Poland.

COUNCIL ON NATIONAL EMERGENCY MEDICAL SERVICE

The following paper is the last of a series of six special articles dealing with the role of the individual physician in medical civil defense planning and operations. These articles will be available in booklet form on request.

C. JOSEPH STETLER, *Secretary.*

THE IMPROVISED HOSPITAL

Harold C. Lueth, M.D., Evanston, Ill.

The improvised hospital is an important link in the medical care program of civil defense. Even with maximal expansion of existing hospitals to two or three times their present capacities, they would be able to provide for only a fraction of the sick and injured after a large-scale disaster. A review of the considerations of location, designation, and floor plans for improvised hospitals might be helpful here to civil defense planning and operation. The important steps of staffing and developing routine management procedures for improvised hospitals must be done well in advance of the actual opening and operation of these institutions. Establishment of improvised hospitals and making provisions for procurement, storage, and replenishment of supplies consumed in active operation are essential steps in providing good medical care for the patients admitted to these hospitals. This report will present lists of suggested duties of physicians, dentists, veterinarians, pharmacists, nurses, nurses aides, and other workers and will briefly outline the place of the improvised hospital within the medical care pattern of civil defense and its relationship to rescue, warden, transportation, communication, and welfare services.

CARING FOR DISASTER CASUALTIES

The Federal Civil Defense Administration is charged with assisting in the provision of medical care of casualties that may follow enemy action or major peacetime disasters. Legislation has been adopted in a number of the states to include the peacetime disaster in civil defense programs, and such action is being considered in others. It is generally recognized that relatively small disasters, involving a hundred or more casualties at one time, severely tax the medical facilities of moderately large cities. This is not surprising, as nearly all normal peacetime medical care is planned on the basis of the reception of small numbers of patients during the usual working hours and working days. Most of the emergency medical treatment facilities of civilian hospitals are designed to accommodate one or several patients at a time. Normally, nearly all peacetime requirements are met by two to six emergency table treatment facilities for each 100 hospital beds. Industrial concerns, special emergency hospitals, and military installations are exceptions to the general rule. A relatively small disaster often completely overwhelms existing hospital facilities and disrupts normal operation.

Facilities for Emergency Medical Care.—Different procedures and techniques in reception, admission, sorting, initial treatment, subsequent treatment, discharge, and disposition will be required in the proper handling of large numbers of patients after a disaster. Disasters that result in several hundreds or thousands of casualties overwhelm existing facilities and necessitate additional facilities for hospital care in readily activated emergency units called improvised hospitals. Emergency medical care, that is, the treatment of shock, arresting of hemorrhage, and necessary initial surgery, are the main features of care that will be given in improvised hospitals. In brief, surgeons working in improvised hospitals set up near the scene of disaster will be able to save lives among those patients who could not stand transportation to distant existing hospitals.

Three medical installations are considered essential in the handling of civil defense casualties: first-aid stations, improvised hospitals, and existing hospitals. After the injured are freed from debris by members of their families, friends, rescue teams, civil defense wardens, and others, they will then be directed to the first-aid station, going unaided or, if necessary, assisted by family or friends. Casualties who need first aid will be treated by members of the family, neighbors, or members of the first-aid team. Those unable to walk will be prepared for litter haul by the litter-bearer teams working out of first-aid stations.

Provisions for Treatment.—At the first-aid station patients will be examined and treated. In general, treatment will be largely confined to stopping hemorrhage, treating shock, treating burns, easing pain, and performing the immediate surgery necessary to save life and limb. Minor wounds, burns, and medical conditions will be treated and the patients dismissed. Those casualties who need it will receive appropriate psychiatric treatment. The seriously injured who require more extensive surgery and who can stand transportation for a short distance will be evacuated to the improvised hospital. Patients who can be transported longer distances or who require specialized care such as eye surgery, neurosurgery, and thoracic surgery may be sent to existing hospitals with these specialized facilities.

SETTING UP THE IMPROVISED HOSPITAL

Location.—Improvised hospitals should be dispersed throughout the metropolitan area, so that several will be near the periphery of the probable damage zone. School buildings, especially the more modern, offer excellent sites as they are fairly readily converted into a hospital; they have large floor areas, water and toilet facilities, electrical wiring, wide stairways and doors, service drives, and ample space surrounding the building. Estimates from the School Housing Section, Office of Education, indicate an average of one school classroom for each 150 persons in a larger city. Most schools are fairly well built and maintained and require a minimum effort to convert to an improvised hospital. Means of feeding patients are existent in schools or could easily be added. Other buildings such as large garages, warehouses, theaters, and church basements could be used, although they do not generally have all the utilities, heating, plumbing, access drives, and other features found in schools.

The closer an improvised hospital can be established to the disaster area and the earlier it can be put in operation, the more effective it will be in saving lives. Experience in World War II and more recently in Korea showed that the farther forward the Army surgical hospitals, mobile (formerly called mobile Army surgical hospitals or MASH units), the greater the saving of lives. No small part of the reduction of mortality of battle casualties from World War II to Korea was the effectiveness of the forward-placed MASH units.

In civil defense, with the probability of a large number of casualties, planning must be far in advance of the event. Traditional military operations permit time as the action develops for the establishment of hospitals. There is also a lapse of time until military casualties are evacuated from forward installations. In civil defense after enemy action, large numbers of casualties may be sustained within a short period of time. Also the large group of uninjured persons will be engaged in a wide-scale evacuation of wounded so that medical installations will soon be deluged with patients. It becomes imperative that locations for improvised hospitals be selected as soon as possible, preferably prior to disaster. Every effort should be made during planning and training phases to make the improvised hospital readily available to the injured and wounded as soon after the disaster as possible.

Designation.—Improvised hospitals should be designated as soon as possible so that they may be included in the civil defense plan. Arrangements must be made with the school board or owners of buildings and property for the use of the buildings for training purposes and during an emergency. It would be well to have conspicuous markers prepared in advance of the disaster,

which would include the designation of the hospital and directional arrows leading to the hospital from the main roads. These signs could be put in place before or immediately after the disaster, thus minimizing confusion and traffic jams. Suitable directional signs and ward or room designations within the hospital should also be prepared in advance and either put in place or stored with the hospital equipment. When stored they must be readily available for use. It is desirable to have wall brackets or fasteners for the signs installed before the disaster. Arrangements should also be made with the school board or owners or trustees of buildings for the storage of supplies and equipment needed in civil defense operations.

Desirable Features.—Floor plans for the improvised hospital will vary with the staff available and the existing buildings. Careful planning and consideration of all details will be required to insure the most effective use of the existing building. Certain general desirable features include a large admission room, several separate rooms for the treatment of shock and burns, and operating rooms equipped with water, sewage disposal facilities, and electric current.

The admitting room or rooms should be at or near the entrance or service drive. It is important that access driveways are semicircular and that traffic flows in only one direction so that vehicles can drive to the entrance, unload casualties, and drive away. Single car-loading platforms must be reconstructed to permit the loading and unloading of several vehicles at one time and to permit an uninterrupted flow of traffic. Provisions must be made in advance to have police officers direct traffic outside the hospital. Experience in recent tornadoes indicated that medical care in hospitals was badly handicapped by traffic snarls outside the hospital, which made it difficult for doctors, nurses, and patients to get to the hospital. Access lanes to the hospital must always be open to permit the ready inflow of new patients to the improvised hospital.

Immediately within the hospital there should be a guide or guides to direct patients and attendants to the admitting room. It is desirable that a floor chart of the hospital be prepared in advance, showing the flow of casualties through the hospital. Patient admission to the hospital should be limited to one entrance to avoid confusion and insure proper reception, record taking, and treatment. Special arrangements may be made in advance to have doctors, nurses, and other hospital personnel enter through a separate entrance, thus minimizing admitting room confusion and permitting free access to professional persons. Immediately after entering the hospital, patients should be referred to the admission room. Clerks here will check medical records that accompany the patient and make suitable entries on the improvised hospital records. Records will be initiated if the casualty has none. When the family or friends accompany the patient, additional data will be secured and recorded. Only one person will be permitted to accompany the patient to the admitting room to give necessary personal information about him. As soon as the information is obtained, the person accompanying the patient will be asked to leave the hospital. Every effort will be made to provide information concerning patients to relatives through the registration and welfare services. Critically injured patients should be grouped in one area of the hospital and suitable arrangements made so that relatives or close friends may visit. Chaplain service and personnel are integral to the improvised hospital.

It is desirable to have interview rooms for the relatives and friends away from the general flow of patients to the hospital, to provide privacy during the interview and reduce admitting room traffic. The importance of securing adequate information from the family and friends can not be stressed too much for medical and social reasons. Large numbers of inquiries are made post disaster, and the earlier full information regarding casualties is available, the more anxiety and panic can be forestalled.

After admission the patient is referred to the examination room where a physician makes an examination and disposition of the case. The examining room should be well lighted, have several examining tables or means on which to rest litters, and adequate diagnostic instruments and supplies. A separate entrance and exit to the examining room are desirable.

There should be special rooms for the treatment of shock, hemorrhage, and burns. Provisions should be made for the separation of men and women patients, and a ward should be designated for children and infants. Operating rooms should both be near to one another and to the sterilization and clean-up rooms. Frequently plumbing installations will, to a large extent, determine the location of the operating rooms. Provisions must be made for the storage of supplies, washing of linen, and cleaning of instruments and equipment. Special facilities for the feeding of patients and hospital personnel must be designated in advance. In many plans, the welfare services have accepted feeding responsibility. A small room or portion of one room must be reserved for laboratory work. Too often the reservation of a room as a morgue is overlooked. Rooms must be set aside for hospital personnel to change uniforms. A lounge or lunch room is a vital necessity for personnel who are required to work long hours under improvised conditions of hospital care.

STAFFING THE IMPROVISED HOSPITAL

The staff of the improvised hospital depends largely on the skill of the professional personnel available. Several surgical teams should be recruited for each of the improvised hospitals. The number of teams is limited by the number of nurses, anesthetists, and assistants available and also by the instruments and equipment available. It is a responsibility of medical societies working with civil defense organizations and with other professional groups to recruit sufficient qualified personnel adequately to staff improvised hospitals. In the interest of maximal utilization of professional personnel, it would seem desirable to use the younger, better physically qualified physicians and surgeons in improvised hospitals and the older and physically handicapped in existing hospitals. A suggestion has been made that, in general, assignments be made largely on the basis of age, so that men over 60 be assigned to existing hospitals, those 45 to 59 to improvised hospitals, and those under 45 to first-aid stations, using the more physically qualified for work under field conditions and the older men in existing installations. The plan should also recognize the military liability of younger men for duty with the medical corps of the armed forces. Each medical society will have to make individual study and assessment of the capabilities of its members in order to meet the problem fairly and impartially. Other professional groups will have to meet the same problems in their respective fields. Local civil defense organizations will coordinate the efforts of the various professional groups with existing local, state, and federal civil defense plans and policies.

When staffs are recruited for an improvised hospital, the professional groups selected should meet and develop an internal organization among themselves. The medical profession has a special obligation in furnishing leadership in the recruitment, selection, organization, and training of the professional complement of the improvised hospital.

DEVELOPING MANAGEMENT PROCEDURES

Routine management procedures should be developed in advance of the opening of the improvised hospital. Disaster is unpredictable, and plans must be flexible enough to meet any situation. It is desirable to have broad plans of operation that are easily understood and capable of being put into operation by semi-trained or untrained personnel. Whenever possible, alternate personnel should be designated for all assignments.

The movements of people in metropolitan areas during day and night have been given special study recently as a part of urban analysis. A study of the professional personnel residing in a suburban city adjoining a large metropolitan center showed that nearly one-half of the night resident physicians left the suburb during the day to practice in the metropolitan center and nearly one-third of the active practitioners of the suburb lived outside the suburb studied.

Larger nuclear weapons with greater radii of destruction make it necessary to place greater reliance on medical support

from peripheral zones. Suburban communities and small outlying communities have distinct obligations in the recruitment, training, and organization of improvised hospitals. At the same time, the urban communities should contribute, both financially and in support of, preparation and training activities of civil defense in the suburban and outlying communities.

After the staff of the improvised hospital has been formed it is desirable to develop a series of routine operational procedures. The outlines, pamphlets, and other materials available through the Federal Civil Defense Administration, the National Research Council, and the various state and metropolitan civil defense organizations are especially helpful. Standing operating procedures should be formulated as a means of using the supplies available and the heterogeneously trained personnel in meeting the needs of medical care for large numbers of casualties. Time and effort spent in the preparation of standing operating procedures will be amply repaid during a disaster by the more effective functioning of the improvised hospital. Written or printed procedural methods, as well as organization charts, floor plans, and traffic flow charts, have the further advantage of serving as guides for personnel hastily recruited or who volunteered their services during a disaster.

The uncertainty that assigned personnel of the improvised hospital will report for duty within specified periods after a disaster is another reason for the desirability of written standing operating procedures. Personnel can be reassigned from one section of the hospital to another and, if given printed routine management procedures, they can be profitably put to work until trained personnel arrive. While there will be some objection to the development of routine procedures on the grounds that some persons can effect better results by their individual procedures, there should always be the greatest latitude possible given to persons within the functioning of medical teams. Maximum individual skills that will combine with the efforts of the rest of the improvised hospital staff in securing the greatest treatment to the largest number of casualties is a safe rule of operation.

ESTABLISHING THE IMPROVISED HOSPITAL

The actual establishment of an improvised hospital is a difficult and time-consuming procedure. Equipment and supplies should be stored and packaged so as to enable the ready access to materials most urgently needed. Unloading, unpacking, and setting up the hospital should follow a prearranged plan. In disaster situations, there will be urgent requirements for the treatment of casualties at the same time that efforts are being made to establish the hospital. It would be well to have one small section of the hospital capable of giving treatment while the remainder of the hospital personnel are busy unpacking equipment and supplies. A plan of this type necessitates considerable detailed preplanning and training for effective operation.

Increased requirements of mutual aid following the development of larger nuclear weapons pose real problems for the improvised hospital. Floor plans should be carefully studied by the improvised hospital staff, so that the hospital can be readily established in new and unfamiliar quarters. A basic operational floor plan and flow charts of patients, supplies, and personnel should be developed at the earliest practicable time. A basic plan can thus be altered to meet any new situation or surrounding. Every effort should be made to find existing structures in the area that lend themselves as possible sites for improvised hospitals. Metropolitan centers and their surrounding areas should be surveyed for locations of improvised hospital sites. Multiple sites should be selected and a single site chosen for the improvised hospital of the community. Other sites will be allocated to improvised hospitals that may be moved into the region by mutual assistance operations.

Procurement and Storage of Supplies.—Supplies for the improvised hospital are available through the federal-state matching plan. Lists of equipment and supplies for the 200-bed improvised hospital have been compiled by the Federal Civil Defense Administration and are readily available. The 200-bed improvised hospital requires at least 18,000 sq. ft. (16 to 17 sq. m.) of floor space. Supplies and equipment weigh about 13 tons and cost about $26,500. Much study and thought have been given to the compilation of lists of equipment and supplies, and the present official list represents the consensus of experienced men in this field. Supplies and equipment reflect current medical practice and procedures.

The storage of supplies requires special precautions. Ample floor space should be available in or near the building to be used as the hospital. There should be sufficient security to prevent losses through theft and pilferage and, at the same time, allow for ready access in case of disaster. Supplies and equipment should be stored in a manner that would facilitate early establishment of the hospital with a minimum of effort.

Replenishment of Supplies.—Supply replacement will be initiated as soon as disaster occurs. State medical directors will use the supplies available to them in their respective states first. As state supplies are exhausted, requisitions will be made to regional medical officers for supplies. Through the federal warehousing program steps will be taken to replenish supplies as they are consumed. The large amounts of supplies needed for a big-scale disaster make it imperative that everyone participating in civil defense medical activities exercise all possible economies in the use of supplies.

Lists of Suggested Duties.—In organizational and training phases of the improvised hospital, it is helpful to devise lists of suggested duties for physicians, dentists, veterinarians, nurses, and pharmacists. The formulation of suggested duties for professional personnel will help clarify the organization and function of the improvised hospital and also provide more easy and rapid integration of additional or new personnel to the professional staffs. Such lists will be more in the nature of check lists of duties and should become valuable aids in crystallizing direction of thought in professional coordination of effort. They should be broad and suggestive and not be considered as detailed or mandatory orders.

COORDINATING FUNCTION WITH OVER-ALL DISASTER PLAN

The improvised hospital is primarily for the care of the seriously injured, nontransportable casualty. Continuous effort must be maintained to select and care only for this type. Minor injuries must be promptly referred to aid stations. If the load of minor injuries becomes too large at the improvised hospital, it may be necessary to establish an aid station near to, but independent of, the improvised hospital. Casualties that can be transported must be evacuated as soon as possible. In order to accomplish its mission, the improvised hospital must be able to accept new casualties of the nontransportable, seriously injured type at all times. It will require skilled work at the admitting room and expert evacuation at the discharge wards to reach this objective. Patients ready for evacuation should be transported to existing hospitals, convalescent areas, or their homes as the circumstances demand and permit.

Proper functioning of the improvised hospital is dependent upon close coordination with rescue, warden, transportation, and welfare services. Rescue teams and civil defense wardens can assist by sending the seriously injured patients to the nearest improvised hospitals. Transportation services are essential in the prompt evacuation of seriously injured to the improvised hospital and removal of these treated from the improvised hospital. In addition, transportation will be helpful in moving personnel, staffs, and supplies to the improvised hospital. Police are essential in maintaining proper traffic flow and avoiding traffic snarls, panic and disorder.

Communication services are especially important in the establishment and functioning of the improvised hospital. Experience in civil disaster has pointed to the great reliance of medical personnel and hospital staffs on adequate communication for augmentation of staffs of existing hospital. The improvised hospital is even more dependent upon proper communication facilities. Some have suggested that the improvised hospital have a portable generator power plant with a radio communication network as an integral part of the hospital. Failure of commer-

cial power and communications would not stop the improvised hospital equipped with this field-type radio net from functioning. Arrangements must be made in advance to include existing hospitals, police, fire, warden, transportation, welfare, and medical services in the radio net.

The welfare services work very closely with the improvised hospital staff. Often welfare services will assume responsibility for registration, clerical assistance, feeding, shelter of discharged patients, and other fields of service to patients of the improvised hospital. Close relations should be developed between the welfare services and the medical staff of the improvised hospital.

BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Medical Practice Acts: Unlicensed Practice of Naprapathy as Violation of Act.—The defendant was charged with three specific violations of the Illinois medical practice act. The first charged that he violated the provision that if any person shall diagnosticate, profess to heal, prescribe for, or otherwise treat any ailment or supposed ailment of another without procuring a license, he shall be subject to penalty. The second charged that he violated the provision that if any person shall attach to his name the title doctor, physician, surgeon, M.D., or any other word or abbreviation indicating that he is engaged in the treatment of human ailments as a business, he shall be subject to a penalty. The third charged that he violated the provision that if any person prescribes treatment for the relief or cure of any ailment of any person with the intention of receiving a fee for the same without first procuring a license, he shall be subject to a penalty. The defendant was found guilty on all three charges in the trial court, and he therefore appealed to the appellate court of Illinois.

At the trial an investigator for the Department of Registration of the State of Illinois testified that he went to the office of the defendant and observed a sign on the building that read, "Ival A. Mainard, D.N."; that he went into the office and said to the defendant that he was looking for Dr. Mainard; that he said, "Are you him?"; and that the defendant replied, "Yes." The investigator further testified that he told the defendant he was Cris Jensen and wanted to get a treatment; that he told the defendant he had trouble sleeping and his legs were nervous; that he asked the defendant if he could help him; and that the defendant answered, "I think so." He testified that in the defendant's office there was a machine about 4 ft. (1.22 m.) long and 2½ ft. (0.76 m.) wide with insulated wire coming from it to a plate about 2½ in. (6.35 cm.) wide; that the machine had printed on it the words "Diagnostic" and "Menograph"; that the defendant worked buttons on the machine while putting the plate on the back of the investigator's neck; that the defendant then took his blood pressure with another machine; that he tested his heart; that he placed various pencil marks on his back and told him he marked them so that he could give him a treatment; and that he manipulated his vertebrae and hips with his fingers on the marked places. The investigator testified that after this, the defendant said cost of the treatment was $3.00; that he asked the defendant if vitamin pills would help him; and that the defendant said he thought they would and asked if the investigator wanted to buy a bottle for $3.50. The investigator testified that he paid the $3.00 and said he would send the $3.50 for the vitamin pills, and that he did this. This was the only time the investigator was in the defendant's office; he said that the defendant told him at that time that his trouble was poor circulation in his legs. The defendant testified that he was a naprapath physical educator, and that this consisted in teaching persons to exercise properly, to breathe properly, to eat properly, and to watch matters that interfere with habits of sleeping and relaxation. The defendant said that the investigator came to his office on the day in question and asked him if he was a naprapath; that he said he was; that the investigator asked him whether or not he was Dr. Mainard; and that he replied, "My name is Mainard. What can I do for you?" The defendant further testified that the investigator told him he had trouble with his legs; that the defendant told him all he could do was to give him a nonmedical treatment; that he would not offer medical service; that no one else was present but the investigator and himself; that he permitted the investigator to take an exercise that consisted in the main of the investigator's lifting his legs in the air and letting them down gradually; that he then proceeded to use electric current from the machine above mentioned in the same manner as the investigator testified; that the purpose of the machine test was to determine if the organs of the body were functioning normally; that he then checked the investigator's heart to determine whether or not it was going too fast or too slow and told him that from the examination of his heart he determined that he could take the exercises he might give him; that the investigator then took the exercises as above mentioned; that the purpose of the exercises was to relax the patient, relax the muscles, and stimulate lazy muscles; and that he told the investigator how to take the same type of exercises at home. The defendant admitted that he gave the investigator what he called passive exercise by manipulating his hands on the body of the investigator in the manner described; that he then discussed with the investigator the proper food to eat; that the investigator asked him if there was any vitamin he could take to help build up his diet; and that he told him he would sell him a package of food that was rich in vitamin B, but he was selling it not to correct any disease but for the purpose of balancing his diet and giving him better nutrition. He further testified that he told the investigator his charge for the exercise was $3.00 and the price of the "food in the package," the vitamin pills, was $3.50, and that he received $6.50 from the investigator. He admitted that he did not have a license.

The purpose of the medical practice act, said the appellate court, is to regulate the treatment of human ailments for the better protection of public health. It is designed to require all persons treating persons afflicted with disease to have a license, so that the public may be protected against the practice of treatment by inexperienced and unqualified persons. The testimony of the investigator and, to some extent, the testimony of the defendant established the guilt of the defendant in that he did prescribe for and treat the supposed ailment of the investigator without procuring a license. The testimony established, said the court, without question that he prescribed treatment of the supposed ailment of the investigator and received a fee for the same. We believe, the court concluded, that the jury was justified in finding the defendant guilty of the first and third charges made against him.

We do not believe that the evidence justifies conviction on the second charge, however. This charge was that the defendant purported to be a doctor by attaching to his name the title Dr., physician, surgeon, M.D., or other word or abbreviation indicating that he was engaged in the treatment of human ailments as a business. The only testimony to sustain this charge is that his office sign had on it "Ival A. Mainard, D.N." We do not believe, said the court, that the use of the letters "D.N." after his name would lead the public to believe that he was engaged in the treatment of human ailments. We do not believe the letters "D.N." should be construed to be synonymous with "Dr., physician, M.D., or other words or abbreviations indicating that he was engaged in the treatment of human ailments."

Accordingly, the conviction of the defendant on the first and third charges was affirmed and the conviction on the second count was reversed. *People v. Mainard, 107 N. E. (2d) 878 (Illinois, 1952).*

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Long-Term Prognosis Following Myocardial Infarction, and Some Factors Which Affect It. D. R. Cole, E. B. Singian and L. N. Katz. Circulation **9**:321-334 (March) 1954.

Of 390 patients who had their first attack of myocardial infarction between 1932 and 1942, 105 died during the first two month period after the attack and 285 who survived were followed up until their death or the end of the authors' study, i. e., up to Jan. 1, 1952. Two-thirds of the 285 patients lived over 5 years after the original infarction, two-fifths over 10 years, and one-tenth over 15 years. Of the 285 patients, 196 who had died after the first two months had lived five and one-half years on the average. The remaining 89 who were still alive at the completion of the study had lived 14 years on the average. The life span for all 285 patients was slightly over eight years on the average. The average life span for the 390 patients was slightly over six years. The average age of the 105 patients who died within the first two months was 60 years, while the average age of the 125 patients who survived longer than 10 years was 53 years. This age differential in favor of long-term survival applied to both men and women. The long-term prognosis is, therefore, better in younger patients. Men were noted to have a slightly better prognosis than women. This difference was probably due to the fact that men were on the average five years younger than the women in the authors' series. Hypertension before or during the attack apparently had no effect on the immediate mortality; its absence definitely increased the long-term survival. Hypertension was more frequent in the older than in the younger age group, and it was more frequent in women than in men, especially in those aged over 60. Diabetes mellitus appearing before or as a complication of the acute attack had no augmenting effect on the immediate mortality, but its presence was a factor against long survival. The claim of other workers that diabetes mellitus is an important factor in leading to myocardial infarction in the younger age groups was not supported by the authors' study. Diabetes mellitus increased the proportion of women with infarction. Women with diabetes lived longer after their infarction than did men. Angina pectoris was present in 234 (60%) of the 390 patients before the first attack of myocardial infarction. The absence of angina pectoris had no effect on the immediate prognosis, and only a slight beneficial effect on the long-term survival. In patients with angina pectoris for at least one year before infarction, there was a reduced immediate mortality and an increased chance for long survival as compared with those who had angina pectoris for a shorter time. Congestive failure during myocardial infarction definitely contributed to increase the immediate mortality. The chance of long-term survival was diminished by the presence of congestive failure at the time of infarction. The presence of shock affected the immediate prognosis of the acute attack in the same way as did congestive failure, but shock had no effect on the long-term survival. Pulmonary embolism was an important factor in increasing the immediate mortality; this complication practically excludes the possibility of prolonged survival. The presence of gallop rhythm during the attack indicated a poor prognosis both for immediate and for prolonged survival. Acute diffuse pericarditis had a negligible effect in increasing the possibility of immediate death and had no effect on the long-term prognosis. Body build had no apparent effect on prognosis. Analysis of the electrocardiogram showed that infarcts of the anterior wall had a better immediate prognosis than infarcts of the posterior wall; the long-term prognosis in the two types was the same. Patients with atypical patterns (excluding subendocardial patterns) and patients in whom the septum was involved had the worst immediate and long-term prognoses. Patients with subendocardial infarct patterns had a good long-term prognosis. Intraventricular block and auriculoventricular block had a slight worsening effect on the immediate prognosis and definitely lessened the chance of long-term survival. The results of the authors' study suggest that the long-term survival time of recent myocardial infarction is better than that previously estimated, especially for the first episode. The implications of this in evaluating the role of prophylactic surgery or medicinal regimens are obvious. The possibility of restitution to full activity is real for many persons surviving a myocardial infarction.

Visualization of Valvular and Myocardial Calcification by Planigraphy. L. A. Soloff, J. Zatuchni and H. Fisher. Circulation **9**:367-370 (March) 1954.

Of 13 patients with valvular heart disease studied for intracardiac calcification, 9 between the ages of 26 and 59 years had rheumatic mitral valvular disease, predominantly stenosis, and 4 between the ages of 52 and 70 years had aortic valvular disease, 3 with stenosis and 1 with insufficiency, but had no history of rheumatic fever. Seven were subjected to mitral valvular surgery, and a diagnosis of calcification was confirmed in each. Conventional roentgenograms taken in the posterior-anterior, right and left anterior oblique, and left lateral views demonstrated calcification in only 2 of these 13 patients, one with aortic and the other with mitral valvular calcification. Roentgenographic study with the Potter-Bucky diaphragm revealed calcification in only two of nine patients, one with aortic and the other with aortic and mitral valvular calcification. Roentgenograms, with the use of a cone, a Potter-Bucky diaphragm, and short exposure time, demonstrated calcification in four of six patients studied, three with mitral and one with aortic calcification. Fluoroscopic studies revealed calcification in 12 of the 13 patients, in 9 calcification being in the mitral valve, in 2 in the aortic valve, and in one in both the aortic and the mitral valve. Planigraphy studies demonstrated calcification in the mitral valve alone in seven patients, in the mitral and aortic valve in three, in the mitral valve and left auricular wall in two, and in the aortic valve alone in one. Surgical experience indicated that conventional roentgenography has a low positive yield. Fluoroscopy has a high positive yield, but has the disadvantages of dependence on individual interest and knowledge and of failure to provide a permanent record verifiable by others. Planigraphy proved to be superior to all other methods in the number of persons demonstrating calcification, but calcification also was more readily recognized in the planigrams, because its shadow stands out in pronounced contrast to the surrounding cardiac densities. It is suggested that planigraphy become a routine study if the detection of intracardiac calcification is regarded as important.

Genesis and Importance of the Electrocardiogram in Coarctation of the Aorta. R. F. Ziegler. Circulation **9**:371-380 (March) 1954.

Electrocardiographic studies were made on 57 patients between the ages of 10 days and 36 years with coarctation of the aorta. Electrocardiographic evidence of right ventricular hypertrophy or right bundle branch block was observed frequently in infants with uncomplicated coarctation of the aorta. 1. Right ventricular enlargement at birth results from the fetal circulatory pattern with the ductus inserting proximal to the region of coarctation. 2. Neonatal right ventricular enlargement and occasionally right-sided congestive heart failure are retrogressive and do not necessitate immediate surgical interference if the

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ductus closes normally at birth. 3. The prognosis in these infants is excellent. Electrocardiographic evidence of left ventricular hypertrophy (and occasionally left bundle branch block) was observed less frequently in infants with uncomplicated coarctation of the aorta than in older children and adults with this defect. The following observations appeared to characterize this group of infants. 1. Left ventricular enlargement and failure are progressive and usually fatal. 2. This sequence of events is believed to represent the pattern of the fetal circulation with the ductus in utero inserting distal to the region of coarctation and closing after birth. The genesis of the electrocardiographic pattern of right bundle branch block in older children and adults with uncomplicated coarctation of the aorta is believed to result, in part at least, from the sequential progression of right ventricular hypertrophy to right bundle branch block as observed when the fetal ductus inserts functionally proximal to the region of coarctation and closes at birth. The same electrocardiographic sequence, from right ventricular hypertrophy to right bundle branch block, was also observed in normal infants and children and in babies with uncomplicated interauricular septal defect. Right bundle branch block is apparently a characteristic electrocardiographic pattern when there is combined right and left ventricular enlargement or when there is anatomic left ventricular hypertrophy and functional right ventricular hypertension. This pattern was observed in coarctation of the aorta with persistent patency of the ductus arteriosus regardless of the exact site of its insertion.

Auricular Fibrillation and Auricular Flutter and Their Treatment by Procaine Amide Hydrochloride. W. Kloppe. Ärztl. Wchnschr. **9**:199-201 (Feb. 26) 1954. (In German.)

Kloppe discusses two theories of the development of auricular fibrillation and auricular flutter and the various therapeutic measures that have been employed, giving particular attention to procaine amide (Pronestyl) hydrochloride. In earlier reports on the use of this drug in cardiac arrhythmias, he observed that it was nearly always given orally or intravenously, never intramuscularly, and also that the majority of investigators emphasized that the drug had a less favorable effect on auricular arrhythmia, such as auricular fibrillation and flutter. Kloppe's own investigations are aimed at ascertaining the value of intramuscular injection of procaine amide and how auricular fibrillation and flutter would react to intramuscular administration. He found that it was best to begin with 5 to 10 cc. (equal to 0.5 to 1 gm.). With this dosage, the rhythm usually became regular in about two hours. A second intramuscular injection was then given 6 to 8 hours after the first one, the dosage being the same. Later oral medication was employed, in which the patients were usually given three times daily 0.75 gm. (3 times 3 dragees). The oral medication is most suitable for maintenance therapy. Eight patients with auricular fibrillation were treated with several large intramuscular doses of procaine amide, but the rhythm could not be regulated. In only one of the cases could a slight improvement be obtained. The results were much more gratifying in auricular flutter. In this respect Kloppe feels that his observations differed somewhat from that of the majority of investigators. These observations demonstrate that it is not always necessary to resort to the intravenous administration of procaine amide, but that intramuscular injection is quite effective. He advises wider use of the intramuscular administration.

Use of Massive Doses (500 to 1,000 Mcg.) of Vitamin B_{12} for Various Conditions Present in Diabetic Patients. P. Dalle Coste and R. Klinger. Policlinico (sez. prat.) **61**:143-149 (Feb. 1) 1954. (In Italian.)

Fifteen patients with diabetes of long standing were given from 500 to 1,000 mcg. of vitamin B_{12} daily to treat various other conditions that were present. Five patients had lumbar and sciatic pain due to lumbosacral arthrosis, two had neuralgia of the fifth nerve, two had pruritus vulvae, and one each had polyneuritis with vertebral polyarthrosis, secondary brachial neuritis, secondary intercostal neuritis, herpes zoster, diffuse psoriasis, and parkinsonian tremor. The study aimed at establishing, in addition to the good effects of the vitamin on these conditions, also the eventual modification of the patients' carbohydrate metabolism and liver function. Diet and insulin dosage were not altered. The vitamin was always well tolerated and never caused toxic effects. Good results were obtained in the patients with conditions of neurotic origin. In these, the pain was substituted at first by a sensation of paresthesia, but this disappeared as the therapy was continued. This phenomenon was ascribed to the direct action of the vitamin on the nervous tissues; it is believed, in fact, that in its physiological mechanism this vitamin uses as a catalytic agent some lipid complexes that are present in high concentration in the nervous sheaths. Gratifying results were also observed in the one patient with herpes zoster and the two with pruritus vulvae. The vitamin had no effect on diffuse psoriasis and parkinsonian tremor. Changes in the carbohydrate metabolism attributable to the vitamin were not observed.

Associated Jejunal and Duodenal Ulcers: Report of Two Cases. K. J. Keeley. South African M. J. **28**:212-213 (March 13) 1954.

Two cases are reported that exhibit the rare association of jejunal and duodenal ulcer in the absence of previous gastroenterostomy. The fact that peptic ulceration is far less common in the Bantu than in the white subject lends additional interest to these cases. Both patients were men in the fifth decade (ages of 42 and 50) who complained of persistent epigastric pain, which was unrelieved by an extensive trial of conservative treatment. The duration of symptoms was three months and six months. They both had good appetite. Bouts of diarrhea were a prominent feature in one. Ascites was present in one and suspected in the other. The ascitic fluid had the characteristics of an exudate; it is suggested that the fluid resulted from peritoneal irritation due to near perforation of the jejunal ulcer. Intestinal parasites were not detected. In the first patient, laparotomy revealed a duodenal ulcer immediately distal to the pylorus that had penetrated the wall and was invading the pancreas. Two inches distal to the duodenojejunal junction, an ulcer had perforated and was lightly sealed off by the adjacent transverse mesocolon. The duodenum was mobilized and closed, leaving the floor of its ulcer attached to the pancreas. The stomach was amputated high up and a Hoffmeister-valve gastrojejunostomy closed. The patient was readmitted on two occasions. He complained of pain in the left hypochondrium but rapidly became pain-free on medical treatment. Barium studies failed to reveal a stomal ulcer. The second patient was subjected to laparotomy because of pyloric stenosis. An ulcer was found in the first part of the duodenum with a stricture reducing the diameter of the lumen to 2 mm. A second ulcer was present just distal to the duodenojejunal junction; it was not exposed, but the crater was palpable through the bowel wall. The ulcer was situated on the mesenteric border and appeared to have penetrated into the mesentery. Partial gastrectomy was performed with end-to-side anastomosis of stomach and jejunum (antecolic, retroperistaltic); a Hoffmeister valve was fashioned. The jejunal ulcer was left, unsutured, proximal to the anastomosis. In view of the duodenal ulcerations, the author feels that the jejunal lesions were peptic ulcers.

The Place of ACTH and Cortisone in the Treatment of Blood Dyscrasias (Present Results). G. Marchal, G. Duhamel, P. Gervais and J. Toulouse. Semaine hôp. Paris. **30**:898-909 (Feb. 28) 1954. (In French.)

Patients with pernicious anemia or chronic myeloid leukemia are not benefited by treatment with corticotropin (ACTH) or cortisone. Patients with other blood dyscrasias may benefit from these agents, sometimes to a marked degree, but the advantages of therapy with cortisone or corticotropin must always be weighed against its disadvantages. Spectacular improvement appears chiefly in the patient's general condition and is shown by euphoria, a greatly increased appetite, and the lessening of fever. The remissions, however, are disappointingly short, and in the malignant disorders recurrences or relapses occur with increasing rapidity and the disease becomes more and more re-

sistant to therapy. Corticotropin and cortisone should not be used, or should be used only with caution, in treating elderly patients or those with hypertension, diabetes, established tuberculosis, or a previous gastric or duodenal ulcer, because severe and unpredictable complications, such as acute pulmonary edema, hemorrhages, intestinal perforation, reactivation of tuberculosis, and episodes of acute infection, not infrequently appear during the course of treatment. Patients should be given a thorough clinical and hematological examination before therapy with these drugs is instituted, and they should be surrounded with all possible precautions while it is in progress. Three years of experience with corticotropin and cortisone in the treatment of 80 patients, 30 of whom had leukoses and 35 Hodgkin's disease, led to the following conclusions: 1. The inconstant and mediocre improvement found in chronic lymphoid leukemia and in agranulocytic syndromes is less than might theoretically be expected. 2. In acute leukemias, the highest percentage of transient remissions was found in forms that affect young persons. 3. Spectacular but transient remissions are frequent in Hodgkin's disease, but there is a constant danger of tuberculous complications. 4. Partial improvement is seen in approximately half the cases of multiple myeloma, though plasmocytic proliferation and hyperglobulinemia usually persist. 5. Prolonged remissions can be secured with cortisone in Brill-Symmers follicular lymphoblastoma and in Boeck's sarcoid. 6. Highly encouraging results have been obtained with therapy with cortisone and corticotropin and transfusions of concentrated washed cells in acquired hemolytic anemia with autoantibodies.

Genotypic Elliptocytosis: Report of 10 Cases. J. Bernard, M. Dugas and M. Cotlenko. Ann. méd. **54:**652-678 (No. 8) 1953. (In French.)

Six of the authors' 10 patients with genotypic elliptocytosis were from the same family, two from another, and two from two separate families in which no other persons with the condition could be found. The disease is a constitutional erythropathy, as are sickle cell anemia, Cooley's anemia, and hemolytic jaundice to which it is most closely related. It is transmitted as a dominant Mendelian trait. It occurs in anemic and nonanemic forms. The authors found that four of their patients had anemia; percentages of anemic cases varying from none to almost 100 have been reported. The anemia may be chronic or transitory. Of the nonanemic types, some are totally latent; their existence is discovered fortuitously unless suggested by family history. Others have a slight hemolytic syndrome. Polyglobulous forms of elliptocytosis have also been reported. Various anomalies are sometimes associated with genotypic elliptocytosis; the authors found none of those reported in the literature, but they were struck by the fact that eosinophilia was present in five of their patients. Two of these could have been due to other causes. In concluding their discussion of the physiopathology of the elliptocyte, the authors state, "It is therefore probable that the cell called elliptocyte is only the form assumed at one point in its life by a special erythrocyte. This erythrocyte is created round, becomes elliptical at the reticulocyte stage, or soon after, lives in this form for several weeks, and becomes round again when it gets old and dies. This special biology of the abnormal cell in part accounts for certain clinical findings." Splenectomy is recommended in severe cases of genotypic elliptocytosis, but, since the clinical symptoms are usually mild, no particular therapy is indicated.

Multiple Myeloma. R. Armas Cruz, F. Valenzuela, R. del Rio and others. Rev. méd. Chile. **81:**593-604 (Oct.) 1953. (In Spanish.)

The authors report on multiple myeloma in six men and seven women. The most frequent symptom was pain in the bones, which appeared in the spine in nine cases, in the thoracic wall in five, and in several joints in two cases. Pain in the spine and in the ribs was acute and of a radiating type. In the joints it was migratory. In three patients, one or more hard painful tumors of the bones were observed, which on histological examination proved to be made up of plasma cells. The roentgen examination of the spine, the skull, the pelvis, and the ribs showed characteristic changes of multiple myeloma in all cases. These consisted of diffuse or circumscribed decalcified areas, softening, deformity of the intervertebral disks, fractures of the vertebrae or of the ribs, osteoporosis, and areas of osteolysis in other bones. Examination of the blood was made in 12 patients. There was macrocytic anemia in six, normocytic anemia in five, and normal values in one patient. Eleven out of the 13 patients presented a syndrome of albuminuria and microscopic hematuria. Bence-Jones proteinuria was present in three patients. In the majority of the patients, uremia was moderately high. In three patients, it was true uremia that progressed to coma in two patients. Nine patients complained of loss of weight and asthenia. Loss of weight was either moderate or rapidly progressive and of apparently unknown origin. The diagnosis in all cases but two was made by cytological or histological examination of the bone marrow taken by sternal puncture. In the other two cases, it was made at necropsy. The myelogram of the 11 patients showed a great increase of plasma cells, up to 15 or 71% of normal. In 10 patients the plasma cells originated from plasmoblasts (the so-called myeloma cells). The finding of plasmoblasts in so high a percentage in the bone marrow is of specific diagnostic value for multiple myeloma, even if no clinical symptoms are present. There was moderate plasmocellular hyperplasia with consequent myelophthisis. Necropsy confirmed the diagnosis in four cases. In two cases, nephropathy of myeloma was observed, whereas in the other two the liver was enlarged and heavily infiltrated by small foci of multiple myeloma.

Protein-Bound Iodine in Serum in Thyrotoxicosis and Myxedema. T. Friis. Ugesk. læger. **116:**329-334 (March 4) 1954. (In Danish.)

The content of protein-bound iodine in the serum in 84 hospitalized patients with various diseases was determined by Barker's distillation method. None of the patients had had roentgen examination with contrast mediums containing iodine, nor had they been treated with expectorants containing iodine during the preceding three weeks. In 31 of the 35 euthyroid patients, the protein-bound iodine values in the serum were between 4 and 8 mcg. per 100 cc., in 3 it was between 8 and 9 mcg. per 100 cc., and in one it was 3.5 mcg. per 100 cc. All but one of the 17 patients with clinically certain thyrotoxicosis showed values over 8 mcg. per 100 cc., four having values between 8 and 9 mcg. The protein-bound iodine values in seven of eight patients with hypothyreosis were under 4 mcg. In a number of cases, determination of the protein-bound iodine in the serum can undoubtedly be helpful in the diagnosis of hyperthyreosis and hypothyreosis in clinically difficult cases. In 11 out of 14 cases observed for hyperthyreosis and in 5 out of 10 cases of suspected hypothyreosis, the diagnosis was supported by the protein-bound iodine values in the serum.

Treatment of Basedow's Disease with Synthetic Estrogens. M. J. Rivière. J. méd. Bordeaux **131:**163-164 (Feb.) 1954. (In French.)

The basis of the author's decision to treat toxic diffuse goiter (Basedow's disease) with estrogens is the now generally accepted idea that the hypophysis plays an important part in the physiopathology of this syndrome. Estrogens have been experimentally demonstrated to have a pituitary-blocking action and perhaps also a peripheral neutralization of thyroxin. The author gives from 20 to 30 mg. of dienestrol daily and from 1 to 1.5 gm. of parahydroxypropiophenone. These are usually combined with sedatives. Men also receive 50 mg. of testosterone every two weeks, for the prevention of mammary disorders, while women are given 25 or 50 mg. of desoxycorticosterone. The present series is composed of 20 patients between the ages of 25 and 50 years, followed for an average of two years. Eighteen of the patients in this series were cured; all of them had been treated within the first six months of the onset of their disease. This period is the optimal one for treatment with estrogen. The

other two patients had been ill for almost a year and had received all sorts of other therapy. They benefited little from estrogen therapy, but were definitively cured by surgery.

Tests for Evaluation of Thyroid Function: Use of Essential Amino Acids in Preoperative Treatment of Toxic Goiter. F. Caluzzi. Minerva chir. **8**:870-881 (Dec. 15) 1953. (In Italian.)

To evaluate the function of the thyroid in patients with disturbances of this gland not only the basal metabolism test but other tests should be made. The author made a critical and comparative evaluation of the tests he performed on 22 patients with toxic goiter. He found that the degree of thyrotoxicosis was directly proportional to the difference between the values of the standard basal metabolism test and those of the same test after muscular exertion. He determined also the blood levels of potassium, calcium, and alkaline phosphatase and found these tests very useful for a clinical and functional evaluation of the patient. These values were always increased. Acid phosphatase and cholesterol did not have a characteristic behavior. The "hypophysis test"—alterations of the arterial pressure and the pulse rate after intravenous injection of extract of the posterior lobe of the hypophysis—was valuable for the evaluation of the balance of the patients' autonomic nervous system. The test was always positive in patients whose neuroendocrine system was altered. He concluded that all these tests, with the exception of that for the determination of the blood levels of acid phosphatase and cholesterol, are very valuable in patients with disturbances of the thyroid because they confirm the results of the basal metabolism test and give a more accurate and detailed picture of the functional state of the gland. Before submitting to surgery the patients with toxic goiter (Basedow's disease) and toxic adenoma of the thyroid (six), Caluzzi treated them with choline and methionine combined with the usual sedatives and liver-protecting drugs. A rapid improvement was observed, and the increased blood levels of potassium, calcium, and alkaline phosphatase were restored to normal. He performed the operation shortly thereafter, and the postoperative course was excellent. All the patients were discharged early, and those seen since had no signs of relapse. Choline influenced noticeably the course of the condition, and, although its mode of action is not clearly defined, the beneficial effects may be ascribed to a liver-protecting activity. Because of its action on this organ, the hepatic parenchyma is placed in the best condition to neutralize not only the action of the toxic substances secreted by the thyroid but also that of other toxic substances that are present in the organism and that in normal conditions are neutralized otherwise. The author suggests that choline be used in the preoperative treatment of all patients with toxic adenoma of the thyroid and toxic goiter.

Two Cases of Poisoning by Marking Ink. H. J. A. Hahn. J. Roy. Nav. M. Serv. **40**:39-42 (No. 1) 1954.

Hahn reports on two recruits in the British Navy who drank a small quantity of the black ink that is used for marking clothes in the belief that it would render them permanently unfit for service. Marking ink contains a high proportion of aniline, and this is considered to have been the poisoning agent. It converts the hemoglobin of the blood into methemoglobin by oxidation, the combined oxygen being firmly bound and not available for tissue oxidation. Hence, the oxygen-carrying power of the blood is impaired. The methemoglobin is not a stable substance and reverts to hemoglobin spontaneously once the poisoning agent is cleared from the system. In untreated patients who survive, this occurs in 24 to 48 hours. In one of the cases reported here sulfhemoglobin was detected in the blood; it is formed by the combination of hemoglobin with hydrogen sulfide from the colon. It is said that this occurs more commonly in constipated subjects. The findings in this case seem to support this theory, as when sulfhemoglobin was found spectroscopically, constipation had been present for five days previously. After the poisoning agent has been removed from the stomach, treatment is aimed at clearing the blood of methemoglobin. This is effected by intravenous injection of methylene blue, which acts by reducing methemoglobin to hemoglobin. The quantity recommended is 1 to 2 mg. of methylene blue per kilogram of body weight. In the two cases methylene blue proved highly effective in relieving the cyanosis, and thereafter recovery was rapid.

Changes in Electrocardiogram During Experimental Anaphylactic Shock. Effect of Cortisone on Electrocardiographic and Hematologic Changes Produced by Anaphylactic Shock. (Two Separate Articles.) G. Bickel and J. Fabre. Helvet. med. acta **21**:71-87 (March) 1954. (In French.)

These two papers study certain aspects of anaphylactic shock produced in rabbits by injection of horse serum. The first reports the electrocardiographic changes seen in the standard and precordial leads of 10 rabbits; they subsequently acted as a control group in the second experiment. In all 10, signs of ischemia appeared, going from slight flattening of the T-wave to typical infarct picture, always a posterior one, with dipping of the S-T segment as much as 6 mm. In nine, an irregular ventricular rhythm was found, with several foci of stimulation. In the 10th animal, the disorder took the form of a bigeminal rhythm in which the sinus and ventricular systoles alternated regularly. Disorders in conductivity were also present—auriculoventricular dissociation, branch block, or pictures suggesting Wolff-Parkinson-White syndrome. Another finding was irregular bradycardia. These disturbances can appear without visible shock. They occur in from 30 seconds to 3 minutes after injection and usually disappear in from 5 to 12 minutes (in one animal 35 minutes), except for the ischemia, which may last longer. Two other groups of rabbits were compared with these 10; 9 received daily intramuscular injections of 4 mg. of cortisone per kilogram beginning the day before sensitization and lasting throughout the experiment, and 4 were given similar injections 28 and 4 hours before shock. A fifth, included in this group, received injections 52, 28, and 4 hours before shock. In the animals treated with cortisone from the beginning of sensitization, the electrocardiographic accidents were absent or greatly attenuated. No infarct images were seen, and ischemia was greatly lessened. Only one animal showed dysrhythmia; it lasted 30 seconds. There were no changes in conductivity. This effect of cortisone was very much less in the four animals that received only two injections. All had disorders of rhythm or conductivity and signs of myocardial ischemia. The one rabbit that received three injections, however, showed no changes in its electrocardiogram. This protective effect of cortisone acts directly on the heart and has no influence on the decrease in white blood cells or on antibody formation.

The Possibility of Influencing the Onset and Course of Traumatic Tetanus with Procaine Hydrochloride. H. Kellner. Medizinische **No. 11**:361-363 (March 13) 1954. (In German.)

Tetanus cultures on small wooden sticks were implanted under the skin of mice and guinea pigs, and the wound was closed by suture. In 50% of the experimental animals, the area adjacent to the incision was injected with 2 cc. of 1% solution of procaine hydrochloride (mice) or 5 cc. of 1% solution of procaine hydrochloride (guinea pigs). Some of these animals were given additional injections of a proprietary solution of procaine hydrochloride in benzyl alcohol (Symprocain) in doses of 0.5 cc. (mice) or 2.5 cc. (guinea pigs). Procaine hydrochloride did not prevent the onset of tetanus; all the animals died. The animals that had received procaine hydrochloride and Symprocain, however, lived longer than the animals not so treated. Local spasms occurred in the treated animals, but were absent in the untreated animals that died during severe generalized spasms. Further animal experiments were performed with various dilutions of 1% procaine hydrochloride solution in a range of 1 to 10. The animals treated with procaine hydrochloride in more dilute solution lived considerably longer than the control animals; the aspect of the disease was also changed in that spasms did not occur in animals treated with a highly dilute solution, and death of the animals resulted from general weakness with bleeding from the nose. Of 39,266 injuries sustained by miners in underground work and treated with the routine

use of procaine hydrochloride at the Brotherhood Hospital in Bochum, Germany, between 1949 and 1953, tetanus occurred after the excision of the wound in only two miners who had sustained bruises of the hands and who had not been given tetanus antitoxin because of the rare underground occurrence of living organisms. Both patients had been operated on after receiving regional anesthesia, and, therefore, the wound itself was not flushed with procaine hydrochloride. Tetanus developed in both patients, but the initial course of the disease was benign in both. One patient made a complete recovery. The other patient had only mild tonic muscular rigidity without spasms, but on the 10th day of the disease there was a sudden rise of temperature to 107.6 F followed by death. Mild bronchitis and obstruction of the greater circulation was revealed by necropsy. The course of tetanus was probably influenced by procaine hydrochloride in both patients. Although procaine hydrochloride proved to be of value, its value should not be overestimated. Procaine hydrochloride is not a sufficient prophylactic agent against tetanus in the treatment of wounds. Careful and thorough excision of the wound according to Friedrich's technique is imperative; tetanus antitoxin must be administered if excision of this type is not possible or in particularly dangerous wounds. Active immunization is employed and is valued more and more as the most effective and sparing prophylactic against tetanus.

Evaluation of Medical and Surgical Treatment of Occlusive Arterial Disease. W. F. Kvale. Proc. Staff Meet., Mayo Clin. **29:**148-152 (March 10) 1954.

Kvale shows that so many therapeutic methods have been proposed for occlusive arterial disease that it is almost impossible to evaluate them on the basis of personal experience. Occlusion of the abdominal aorta, thromboangiitis obliterans, and arteriosclerosis obliterans constitute the three major diseases affecting the peripheral arteries. The following principles apply to the treatment of these diseases; (1) arrest the progress of the disease, (2) dilate uninvolved arteries and arterioles, (3) increase circulation mechanically, (4) relieve pain, (5) instruct in prophylaxis against injury of ischemic tissue, and (6) treat ulceration and gangrene. The best management is achieved through the cooperation of the internist, orthopedic surgeon, neurosurgeon, and general surgeon, since medical and surgical methods are supplementary and not competitive. There is no particular difference between the treatment of thromboangiitis obliterans and arteriosclerosis obliterans. The tissues of the extremities in arteriosclerotic patients have less capacity to heal, ischemic neuropathy is more common, and the prognosis as to life and after surgery is poorer because of the greater tendency toward thrombosis in visceral and peripheral arteries. These factors may influence the choice of procedures and also the duration of conservative treatment when gangrene is present. The author comments on procedures to arrest the progress of disease, procedures used for vasodilatation, and procedures used in the treatment of ischemic ulceration and gangrene. In the last few years, several new methods of medical treatment have been advocated, but the results have not been generally confirmed. Heparin appears to have no effect on blood fats nor does it abate intermittent claudication. The subcutaneous injection of hexamethonium bromide may be helpful in selected cases. A sympathomimetic compound tolazoline (Priscoline) hydrochloride is a vasodilating drug, but thus far its value in occlusive arterial disease is doubtful, and it sometimes causes disagreeable side-reactions. Many drugs improve the peripheral arterial circulation temporarily, but continuous long-term drug therapy does not appear feasible. Surgical sympathectomy remains the method of choice for increasing the circulation to the skin of the extremities. The author prefers surgical sympathectomy to medical treatment except in cases in which the general condition of a patient imposes a surgical risk, and in instances in which the arterial circulation is not sufficiently jeopardized to warrant sympathectomy. Chemical sympathectomy is justifiable when the risk of a surgical sympathectomy seems too great, and when vasodilatation is desired for several weeks or months. Drugs are preferable to sympathectomy in acute arterial occlusion.

SURGERY

Surgical Treatment of Peptic Ulceration and Stricture of the Lower Esophagus. R. H. Sweet, L. L. Robbins, T. Gephart and E. W. Wilkins Jr. Ann. Surg. **139:**258-268 (March) 1954.

Of 30 men and 20 women with peptic ulceration and stricture of the lower esophagus operated on, 2 were boys aged 16 years, but most of the patients were in the latter decades of life, 13 between the ages of 51 and 60, 19 between the ages of 61 and 70, and 4 over 70. Thirty patients had symptoms for 5 years or less, 7 for 6 to 10 years, and 7 for 11 to 40 years; the duration of symptoms was unknown in 6. Forty-eight of the patients had a short esophagus type of hiatus hernia with a thoracic segment of stomach, and in 31 the condition was recognized as such by roentgenologic examination before the operation. The principal indications for resorting to surgical treatment were obstruction in 33 patients, pain in 7, bleeding in 3, perforation in 1, and a combination of these in 6. Four operative procedures depending on the severity and extent of the lesion were used in the surgical treatment. One patient underwent a limited esophagectomy, 33 extensive esophagectomy, 8 extensive gastrectomy, and 8 esophagoplasty. There were four postoperative deaths in the hospital. Of the five patients who died some years after the operation, a satisfactory follow-up was made to the time of death in three, and two were lost to observation. Of the remaining 41 patients, 35 were followed up long enough to make evaluation possible. Twenty-six of these obtained an excellent result, 6 obtained a good result, and only 3 had therapeutic failures. Recurrent esophagitis occurred in three patients, and in four transitory dysphagia suggested that esophagitis had been present but subsided of itself. The evidence presented bears out the impression that resort to surgical measures should never be deferred in any case of ulcer or stricture of the esophagus in which there is a history of bleeding, obstruction unsuccessfully treated by bougienage, intractable pain, or, in some instances, evidence of perforation. If a careful choice of operative procedure is made to suit the conditions encountered and the age and physical status of the patient, a satisfactory clinical result can be anticipated in at least 90% of the patients. A diagnosis of recurrent esophagitis after operation can be established only on the basis of roentgenologic and esophagoscopic examination, but the definitive proof of the diagnosis depends on the use of the esophagoscope. It is not possible to decide whether, in cases in which a resection is required, the results obtained by extensive proximal partial gastrectomy will be superior to those obtained by esophagectomy at a high level and a more conservative handling of the stomach.

Results of Gastric Resection in Young Ulcer Patients. K. H. Køster and J. Foged. Ugesk. læger. **116:**197-205 (Feb. 11) 1954. (In Danish.)

In Bispebjerg Hospital from 1942 to 1953, 80 patients with gastric or duodenal ulcer, aged from 16 to 30, underwent Billroth 1, Billroth 2, or Wangensteen procedures. Duodenal ulcer predominated. More than half the patients had had ulcer for six years or longer; hemorrhage or perforation had occurred in half. The indications for operation were history of ulcer for at least a year, at least one completed course of medical treatment in a hospital, roentgenologically demonstrable ulcer, and reduced working capacity. Considerations of possible complications and social and psychic relations also played a part in the decision for operation. One patient died postoperatively, and 16 patients were observed for less than two years. During the observation period of from 2 to 11 years, one patient emigrated and two died, one from secondary ulcer and one through suicide. Of the remaining 60, 58 were free from pain and fully able to work; 51 had gained weight; and 9 had lost weight. Twenty patients had the dumping syndrome after hypertonic food, but all could control their symptoms by avoiding certain foods. The investigation indicated that good results follow gastric resection for ulcers in young patients in whom medical treatment has been unavailing.

Carcinoma of Finger Resulting from Wood Sliver. V. S. Falk Jr. Wisconsin M. J. **53**:187-190 (March) 1954.

While a 60-year-old man was working with old wooden flooring, a sliver was forcibly driven under the nail of his right index finger. The sliver ran the full length of the center of the nail and penetrated the nail bed. The man immediatey extracted the sliver leaving what he thought was only a black mark. He experienced no difficulty until about one year later when the finger began to ache, and he consulted his family physician. Removal of the nail revealed necrotic tissue near the nail bed, which when cleaned out left a rather deep ulcer. Six weeks later, the wound had healed, but the original "black mark" persisted. One year later the man consulted the author. By this time (27 months after the initial injury), the distal phalanx of the finger had become a fungating, bulbous, malodorous mass, and there was some involvement of the middle phalanx. Roentgenography revealed that the bony structure of the distal phalanx was almost completely destroyed. Amputation through the proximal interphalangeal joint left sufficient uninvolved skin of the middle phalanx to cover the stump. Examination of the surgical specimen revealed squamous cell carcinoma. The literature on carcinoma of the hand is briefly reviewed. This lesion is characterized by a long chronic course, often ulcerating for a year or two. The ulcer or cauliflower mass enlarges slowly, involving the adjacent skin and subcutaneous tissue. Eventually tendon, bone, and muscle are invaded. Involvement of lymph nodes is often late and may occur two to three years after onset of ulceration. The presence of nodes does not necessarily indicate metastases, since infection is often the cause. Pathologically the majority of these tumors are squamous cell carcinomas, the remainder basal cell. The prognosis in these cases is relatively good because of the long, slow course before extension and metastases occur. Prophylaxis consists of the eradication of all types of chronic irritation or infection. Attention to warts, nevi, keratoses, old scars, granulomas, and ulcerative lesions is essential. If changes, such as scars from burns or roentgen dermatitis result in malignant degeneration, the involved skin should be removed and replaced by normal healthy skin. Once a cancer has developed, early and radical removal is essential. Irradiation may be helpful when the condition is inoperable.

Operations for Coronary Artery Disease. C. S. Beck. J. Internat. Coll. Surgeons **21**:314-321 (March) 1954.

Experiments carried out by Beck and his associates on dogs demonstrated that occlusion of the descending coronary artery and the circumflex coronary artery intercepts blood supply to the cells of the heart muscle resulting in the development of a dry area or an ischemic area in the myocardium that can destroy the coordinated heart beat. The remainder of the heart is capable of continued function. This type of occlusive disease has its counterpart in human beings, many of whom die from this trigger mechanism, with acute heart attacks. A small amount of blood, as little as 1 to 5 cc. per minute delivered to a trigger area, can remove the destructive nature of this trigger. The physiological mechanisms that can protect the heart against the effects of occlusion of the coronary artery are (1) a more even distribution of the blood that enters through the diseased coronary arteries and (2) an actual increase in arterial inflow. Two operations are presented for conorary artery disease that are referred to as Beck 1 and Beck 2 operations. The Beck 1 operation consists of exposure of the heart. The surface of the heart and the lining of the parietal pericardium are abraded by metal burrs. Powdered asbestos (0.2 gm.) is applied to these surfaces as an inflammatory agent. The coronary sinus is ligated on a probe that has a diameter of 2 mm. The probe is removed from the ligature so that the sinus is not completely occluded. The mediastinal fat is brought in contact with the fat on the heart and also in contact with heart muscle. These structures become adherent. This operation provides definite benefit to the heart in the presence of coronary artery occlusion. The Beck 2 operation is done in two stages. A short graft of vein is placed between the coronary sinus and the aorta, or a direct anastomosis is done. Three weeks later the sinus is partially ligated. This operation adds new blood to the heart. It also produces intercoronary arterial communications. The author's tests showed it to be more beneficial than the Beck 1 operation. It is more difficult to do, and there are some conditions that preclude it. One of these is an atheromatous aorta, and another is the absence of a coronary sinus or the presence of a delicate, friable sinus that cannot be used surgically. Still another condition in the presence of which the Beck 1 operation is preferable to the Beck 2 operation is arterial hypertension (systolic pressure over 160 mm. Hg). One hundred twenty-five patients were operated on. Of those whose condition could be evaluated, 81% had excellent or good results. An excellent result means no pain, no medication, and return to former work. A good result means occasional pain, occasional medication, and return to former work. These two operations can save life, as was experimentally proved. In human beings there is a trend in this direction. These operations also reduce infarction.

Treatment of Thyroid Diseases. A. S. Jackson. J. Internat. Coll. Surgeons **21**:344-350 (March) 1954.

Based on his experience with antithyroid drugs over a period of eight years in the surgical treatment of 700 patients with hyperthyroidism, Jackson adheres to the following indications for the use of these drugs: advanced multiple toxic adenoma in patients who do not respond to iodine; in toxic adenoma complicated by myocarditis, fibrillation, hypertension, diabetes, and decompensation; in severe toxic diffuse goiter of the very young, the aged, the debilitated and the decompensated; in toxic diffuse goiter in patients in whom, because of pregnancy, previous nerve injury, infection, or other disease, it may be desirable to delay surgical intervention and yet not continue the administration of iodine; in iodine-fast toxic diffuse goiter; and in recurrent or persistent hyperthyroidism. The antithyroid drugs have accomplished in the preoperative treatment of toxic adenoma what strong iodine (Lugol's) solution did with toxic diffuse goiter and what iodine failed to do with toxic adenoma. The antithyroid drugs are not comparable to thyroidectomy in the treatment of toxic diffuse goiter in adults, because of the length of time required and the tendency toward relapses. In children these drugs have given encouraging results when used over a period of several years. In all but one of 17 children the disease was controlled, and 4 of them appear to be cured at the time of writing. Radioactive iodine has given encouraging results in the treatment of toxic diffuse goiter and cancer of the thyroid. There was, however, a considerable number of cases of persistent hyperthyroidism, severe exophthalmos, pronounced growth of the thyroid and some cases of myxedema. Radioactive iodine is definitely not indicated for toxic adenoma. Final evaluation of its value has yet to be made. Surgical treatment of the thyroid may be expected to give as excellent end-results and as low mortality rate as any type of surgery, if the operation is performed without prolonged preoperative delay and under ideal conditions. Important factors in the preoperative and postoperative care of hyperthyroid patients are psychological preparation for the operation and preoperative medication, and the requirement to refrain from stimulants such as coffee and nicotine permanently after the operation.

Esophagoaortal Hiatus Hernia. H. D. Adams and A. W. Lobb. New England J. Med. **250**:143-147 (Jan. 28) 1954.

Adams and Lobb recognize a type of hernia that is a subclassification of the esophageal hiatus hernia and is associated with a high incidence of reflex cardiorespiratory symptoms. This herniation through the diaphragm takes place through a defect extending anteroposteriorly from the esophageal hiatus to the aortal hiatus. This muscular defect results in a herniation that extends through the esophageal hiatus into the mediastinum behind the heart. As it enlarges, it is limited above by the hilar structures and expands into each half of the thorax, overlapping the cardiac shadow on either or both sides. In addition to the gastrointestinal complaints associated with hiatus hernia, the major presenting symptoms simulate those of respiratory tract or cardiac origin. There is angina-like pain, cough and wheezing simulating asthma. The surgical approach to this defect in the diaphragm is accomplished with the patient in the lateral position, left side up. A posterolateral incision is made, the eighth rib removed, and the ninth rib cut posteriorly. When the

pleura is opened the herniation may not be visualized; it frequently is obscured within the mediastinum. The phrenic nerve is crushed, and the mediastinal pleura is opened behind the inferior pulmonary ligament. The hernia is dissected from the mediastinum behind the heart, with precautions not to open the opposite pleura, which is usually adherent to deeply situated hernias of this type. Once the esophagus has been identified, the lower end of this structure and the hernial sac are freed and delivered from the mediastinum; the diaphragm can then be cleared of areolar tissue and the defect identified. The defect will be found extending posteriorly from the esophageal to the aortal hiatus with the right crus of the diaphragm lying medially and the left crus forming the lateral rim of the defect. Since these are sliding hernias, it is not essential to remove the peritoneal sac, but it must be opened to ensure that the stomach can be freely reduced into the abdomen and not compressed or "accordionated" below the diaphragm, which may lead to recurrence. The distal end of the esophagus is placed anteriorly in the hernial defect against the firm decussation of the crura and tacked there to maintain it in its proper relation until the repair is completed. Starting at the posterior limit of the defect, at the aorta, heavy interrupted sutures are placed through the edges of the right and left crura and the defect closed progressively anteriorly until the posterior edge of the esophagus is reached. The last stitch next to the esophagus should bring the diaphragm up snugly around this structure so that only the tip of the index finger can be introduced alongside it. The mediastinal pleura and the thorax are closed, an intercostal catheter for suction being left to help rapid reexpansion of the lung. Suction is continued with a Levin tube for 48 hours postoperatively. There has been complete relief of cardiorespiratory symptoms in the eight cases with esophagoaortal hernia in which this repair was carried out.

Occult Carcinoma of the Breast. H. W. Owen, M. B. Dockerty and H. K. Gray. Surg., Gynec. & Obst. **98**:302-308 (March) 1954.

"Ocult carcinoma of the breast" implies histologically proved carcinoma of the breast with axillary nodal involvement in a patient without signs or symptoms of any abnormality of the breast. The authors studied the clinical and pathological material from cases of this type observed at the Mayo Clinic from 1907 through 1950 and compared these data with those obtained from a study of carcinoma of the breast in general. The clinical, operative, and pathological records of 5,451 cases of histologically proved carcinoma of the breast in which there was axillary nodal involvement were reviewed. Twenty-seven of these had occult carcinoma of the breast. Two of this group were subsequently excluded because the specimen that contained the primary lesion of the breast was not available. The incidence of occult carcinoma of the breast was slightly less than 0.5%. Since involvement of the axillary nodes is encountered in about 66% of all cases of mammary carcinoma at the Mayo Clinic, it is assumed that approximately 0.3% of patients with carcinoma of the breast have the occult form. The group of 25 included one man. The authors were unable to find another report of occult mammary carcinoma in a man. There were no symptoms referable to disease of the breast in 24 of the 25 cases. One patient had a slight watery discharge from the nipple for two years prior to radical mastectomy. The axillary enlargements had been noted for less than six months by 22 patients, while the remaining 3 had noted enlarged nodes for more than two years. A biopsy of the axillary nodes in 22 patients was followed by radical mastectomy. Two patients had a "primary" radical mastectomy without previous biopsy of the axillary nodes, and one had a semiradical mastectomy without previous biopsy of the axillary nodes. Nine of the 25 patients are dead. Six patients of the group have survived 10 years or more and 4 patients have survived 15 years or more without recurrence of the carcinoma. The longest survival with recurrence was 10 years and 3 months, and the shortest survival with recurrence was 10 months. The diameter of the breast lesions was less than 2 cm. in all patients and less than 1 cm. in 60% of cases. A large percentage of the lesions were of the comedo type, and a significant number demonstrated the so-called inflammatory reaction about the tumor. All but two of the tumors were of grade 3 and grade 4 malignancy, but the prognosis was good as compared with that of carcinoma of the breast with nodal involvement in general.

Occult Carcinoma of Breast. R. B. Davidoff. Geriatrics **9**:128-129 (March) 1954.

Davidoff feels that it is not sufficiently appreciated that a primary malignant focus in the breast, so minute as to escape detection, may produce bulky axillary metastases. To 13 cases of this type previously reported by three different investigators, the author adds 6 more that he detected among about 800 cases of carcinoma of the breast. The first of the six cases occurred in a 64-year-old woman. The breast was thin, atrophic, and so easily palpated it seemed impossible that it could harbor a carcinoma that could not be felt. Extensive investigation failed to reveal a primary site. An axillary dissection, without removal of the breast, was done. Eighteen months later, a 1 cm. mass was discovered in the breast, which proved to be the primary source, and a radical mastectomy was performed. The patient died of widespread metastases three and one half years later. The 18 month delay in carrying out radical mastectomy may have contributed to the outcome. In the other five cases radical mastectomy was done as soon as the lesion in the axillary nodes had been identified as metastatic adenocarcinoma. In each instance, the pathologist was able to discover a minute primary focus in the resected breast. In one patient, a primary carcinoma developed in the remaining breast eight years after the first operation. Three patients are alive and free of disease 18 to 54 months after surgery. One patient is alive, but with pulmonary metastases three years after operation. The prognosis in occult carcinoma of the breast seems to be that of any carcinoma of the breast in which axillary node involvement is present.

Swelling of the Arm After Radical Mastectomy: Clinical Study of Its Causes. W. T. Fitts Jr., J. G. Keuhnelian, I. S. Ravdin and S. Schor. Surgery **35**:460-464 (March) 1954.

In the five year period between July, 1946, and July, 1951, Fitts and associates performed radical mastectomy on 130 patients with cancer of the breast. The operation consisted of removal of the breast, the pectoral muscles, and axillary contents caudad to the axillary vein, which was not ligated in any instance. Primary skin grafting was performed in 14 instances. At examinations subsequent to operation, special attention was paid to swelling of the arm. Some swelling developed in 49% of the 130 patients. It could not be traced to one determining factor, although several factors that might relate to lymphatic obstruction appeared important. The number of axillary lymph nodes removed, marginal necrosis, and obesity appeared to be the most important. Other factors that might be related to lymphatic obstruction—percentage of lymph nodes involved with cancer, fever after operation, fluid collection, and infection—were only slightly higher in the group with swelling. Penicillin given prophylactically to the majority of these patients did not reduce the incidence of swelling. Other recent reports indicate that the incidence of swelling of the arm after radical mastectomy varies from 8 to 95%.

Use of the Thoracoscope in the Diagnosis of Certain Intrathoracic Neoplasms. C. L. Geraci and L. G. Brizzolara. J. Thoracic Surg. **27**:266-270 (March) 1954.

Thoracoscopy with biopsy of suspicious pleural nodules or plaques may be useful in establishing a histological diagnosis in certain cases of intrathoracic malignancy, thus saving the patient the morbidity and expense of an exploratory thoracotomy. It should not be used in cases in which an apparently operable lesion is present, because it might result in contamination of the pleural cavity with tumor cells. The procedure, which is simple to perform and well tolerated, can be carried out in any center where a thoracoscope is available. The patient is placed in a supine position or with the affected side slightly elevated; local anesthesia is secured; and the thoracoscopic trocar and sheath are introduced through the most appropriate interspace. Pneumothorax is established after entrance into the

pleural cavity by removing the trocar from the sheath. All fluid is drained from the pleural cavity by suction through a small catheter, the telescope and light are then introduced, and the cavity is carefully inspected. The diaphragm and the visceral and mediastinal pleural surfaces can be well visualized, and adhesions, nodules, fluid, or other abnormalities can easily be seen and studied. Insertion of a second trocar and sheath through an adjacent interspace permits the taking of biopsy specimens with an appropriate forceps. Areas of shaggy fibrinous exudate on the pleural surfaces have been found on biopsy to contain nests of malignant tumor cells on several occasions, even though they did not in themselves suggest tumor. Direct biopsy of the intact and apparently normal visceral pleura, however, is not advisable because of the possibility of perpetuating the pneumothorax. Reexpansion of the lung on completion of the examination is secured by suction through a small catheter inserted into the pleural cavity through one of the trocars (usually the upper one) prior to their removal. The catheter is withdrawn when reexpansion of the lung is complete. An accurate histological diagnosis was established by this method in five consecutive cases of obscure pulmonary disease in which other diagnostic procedures had proved inconclusive.

NEUROLOGY & PSYCHIATRY

Procaine Injection of Globus Pallidus in Parkinsonism. I. S. Cooper. Psychiatric Quart. **28**:22-23 (Jan.) 1954.

The effect of occlusion of the anterior choroidal artery in alleviating certain disabilities of far advanced parkinsonism had been confirmed by several investigators. Since the neural structure most consistently dependent on the anterior choroidal artery for its blood supply is the medial segment of the globus pallidus, it occurred to Cooper to develop a technique that would permit injection of procaine into this structure for diagnostic purposes. In two cases, injection of procaine into the substance of the brain in the region of the medial segment of the globus pallidus resulted in immediate cessation of tremor in the contralateral extremities, with alleviation of rigidity as well. Tremor and rigidity remained absent for over 24 hours. Further studies on the injection of longer-lasting neurolytic agents are in progress.

Prognosis in Intracranial Sacculate Aneurysms: After-Examination. E. Frantzen and N. J. Krenchel. Nord. med. **51**:130-134 (Jan. 21) 1954. (In Danish.)

From 1935 to 1952, 73 patients, 33 men and 40 women, with certain intracranial sacculate aneurysms were admitted in the neurological department of the Rigshospital. The aneurysms were demonstrated by arteriography, at operation, or at necropsy. The commonest location was the internal carotid artery. Intracranial surgery was performed in 43 patients and ligation of the common carotid in 4. There were 12 postoperative deaths. Study of the later fate of the survivors, observed for up to 15 years, revealed that 7 patients died from recurrent bleeding, 2 died from intercurrent diseases, 8 were unable to work, 7 were partially able to work, and 11 were fully able to work. Of the 35 not operated on, 13 were living. Muscle covering of the aneurysm in 15 cases gave good immediate results, with only one postoperative death, but five of the patients died before the end of the observation period. The lines of guidance for future operative treatment call for abandonment of purely palliative operations in favor of the more radical and more satisfactory method, ligature of the neck of the aneurysm. Application of hypotensors during the operation will contribute to better results.

Histological and Chemical Study of Three Cases of Diffuse Cerebral Sclerosis. W. Blackwood and J. N. Cumings. J. Neurol., Neurosurg. & Psychiat. **17**:33-49 (Feb.) 1954.

This paper records histological and chemical examinations in three cases of diffuse cerebral sclerosis diagnosed on macroscopic examination. The cases were (1) "spongy degeneration" of the cerebral white matter (Canavan); (2) perivascular islands of residual myelin (Pelizaeus-Merzbacher); (3) numerous "globoid" bodies or "epithelioid" cells in the white matter (Krabbe). Brain tissue of these patients with diffuse cerebral sclerosis was examined, both histologically and chemically, but only one spinal cord was available for histological examination. The brain and the spinal cord from an example of the "spongy type" (Canavan) showed histological features similar to those previously reported, while the chemical findings suggested an arrest of myelination of the cerebral white matter during late fetal life. The second case, an example of the Pelizaeus-Merzbacher type, showed histological features typical of this disorder. Chemical analysis revealed a probable arrest of myelination of the white matter in early childhood, but with a more mature cortex that showed recent degeneration. The last case, one of the Krabbe type, showed histologically typical "globoid bodies." The material in these bodies was found chemically to be cerebroside and this substance had excited a microglial reaction.

Therapy in Epilepsy. F. M. Forster. M. Ann. District of Columbia **23**:137-141 (March) 1954.

According to Forster epilepsy is the most important neurological disease, because it is chronic and one person out of every 200 of the general population has seizures. It is only the unusual patient who is refractory to therapy, or who presents a diagnostic problem that comes within the realm of the neurologist. The type of medication depends on the type of seizure. The author lists the types of anticonvulsant drugs, such as the hydantoinates, oxazolidines, barbiturates, acetylurea, and the like. He also lists the standard drugs according to their indications for the various types of seizures. The value and toxicity of the various drugs is discussed. Although the future outlook is favorable as far as drug therapy is concerned, the social and economic problems encountered by the epileptic patient are still far from solved. Efforts should be made to offset the stigma that is still attached to this disease. It results in difficulties in job placement, school placement, mate selection, and other avenues of social intercourse. The epileptic is a normal person the great majority of the time. The man who has two seizures a year is perfectly competent except for 10 minutes twice a year. The restrictions are not only in the minds of the people but in the lawbooks. The American Epilepsy League is now taking an active interest in this field.

Electroencephalogram in Pernicious Anaemia and Subacute Combined Degeneration of Cord. J. N. Walton, L. G. Kiloh, J. W. Osselton and J. Farrall. Electroencephalog. & Clin. Neurophysiol. **6**:45-64 (Feb.) 1954.

Walton and co-workers report an electroencephalographic survey of patients with pernicious anemia carried out in Newcastle upon Tyne. The 140 cases included 10 of anemia other than the pernicious type; 80 cases of pernicious anemia, first studied while in relapse; and 50 cases of pernicious anemia that had been under treatment for varying periods. Vitamin B_{12} by injection was eventually used in all cases of pernicious anemia, although a number of other remedies were given for brief periods to some patients. The electroencephalogram showed significant abnormality in only one of the 10 patients with anemia other than the pernicious type, and this patient had severe hypertension and atherosclerosis. Of the 80 patients with pernicious anemia in relapse, 24 had subacute combined degeneration of the cord and 41 had mild and 15 no neurological involvement. Seven patients showed mild organic reactions and in all of these the pretreatment electroencephalographic record was abnormal. The pretreatment record was also abnormal in 60% of the remaining patients who showed no significant mental abnormality. In some cases abnormality was severe (delta activity, generalized, paroxysmal, or focal) and in some slight (moderate excess of theta activity), but the degree of abnormality bore no relationship to the severity of the anemia, the age of the patient, or the degree of neurological involvement. Seventy-six of the 80 patients were reexamined after treatment with vitamin B_{12}. In 14 of the 29 with normal electroencephalographic records before treatment, there was a significant increase in mean frequency of the alpha rhythm and diminution in over-all amplitude. Forty-two of the remaining 47 patients in whom the initial record was abnormal showed a satisfactory clinical response to treatment and in 31 the

record returned to normal, so that 60 of the 76 cases eventually gave normal electroencephalographic records. Improvement in the record began as a rule 7 to 10 days after the onset of treatment and was often complete within a month, although some cases showed further improvement after intervals varying from 3 to 16 months. In the other patients who responded, a slight excess of generalized theta activity persisted, which in some could be accounted for by age or constitution. Fifty patients with pernicious anemia (including 37 with subacute combined degeneration of the cord, 8 with mild neurological involvement, and one with optic atrophy) were first studied after treatment had been in progress for between 3 months and 8 years (average 18 months). Excluding five cases showing epileptic discharges, 38 of the other 45 patients had normal records; the remaining 7 were restudied and in all the electroencephalograms showed further improvement five months to three years after the beginning of treatment. It is suggested that electroencephalographic changes in pernicious anemia are due not to the anemia but to a defect in cerebral metabolism, presumably related to the deficiency state responsible for the anemia. Though not as sensitive as studies of cerebral metabolism by the blood flow method, the electroencephalogram is a useful tool and reveals that maximum improvement may be delayed for up to three years after treatment has begun.

Electroencephalographic Studies in Posthypoglycemic Coma. C. L. Yeager, A. Simon, L. H. Margolis and N. R. Burch. J. Nerv. & Ment. Dis. **118**:435-441 (Nov.) 1953.

In the course of insulin therapy for schizophrenia, the patient occasionally continues in a state of altered consciousness beyond the calculated time for termination of treatment. In order to obtain further information concerning alterations in cerebral function in such a state, serial electroencephalograms were made by Yeager and associates in 12 patients with so-called posthypoglycemic coma, which is also referred to as prolonged coma, protracted coma, protracted shock, hyperglycemic coma, and nonhypoglycemic coma. It persists in insulin shock therapy for an indefinite time after the blood sugar has been raised to hyperglycemic level. In the 12 cases reviewed here, the comas varied in length from one to 20 hours. In contrast to the routine treatment comas, the electroencephalogram in these cases showed persistent abnormality for many days after recovery from the coma. There was a close correlation between the length of the coma, organic confusion, remission of mental symptoms, and the degree of abnormality in the tracing. The electroencephalogram did not portend the posthypoglycemic coma. The posthypoglycemic coma was not considered as an indication to terminate insulin treatment. It is postulated that the posthypoglycemic coma is a convulsive phenomenon that leads to an isoelectric condition across the semipermeable membranes of the neurones. The isoelectric condition is felt to be a postictal exhaustion state resulting from an excessive electrical discharge of highly suppressed cells. It is felt that interruption of coma could be brought about by the reestablishment of potentials across the membranes that would again permit cellular exchange of metabolites. The administration of anticonvulsants during insulin therapy might in some instances function as a safeguard against posthypoglycemic coma.

Subconvulsive Intravenous Metrazol Therapy in Mental Patients: Preliminary Report. A. L. Lieberman. Geriatrics **9**:125-127 (March) 1954.

During the last few years pentylenetetrazole (Metrazol) has been employed with good results as a general analeptic for geriatric patients, especially for those with cerebral arteriosclerosis and mental confusion. Lieberman employed intravenous injection of subconvulsive doses of pentylenetetrazole in 75 geriatric patients with arteriosclerotic mental changes. About 50% of these patients showed an excellent response, 25% good response, and the rest poor or no response. Results were measured solely by clinical criteria. The technique employed was as follows: 1 cc. of pentylenetetrazole was given intravenously, with the patient lying quietly in bed. A day or two later, the dose was increased to 1.5 cc. and then to 2 cc. If no reaction occurred, it was increased by 0.2 cc. each time until the dose produced a mild but recognizable reaction. This reaction usually consisted of a slight twitching of the body, blacking-out, or even a mild convulsion with a period of unconsciousness lasting from 5 to 15 seconds. This established the necessary dose and subsequent doses were kept just below this level. The patient received 25 to 50 such intravenous injections at intervals of two to three days. At the end of this series, injections were given only once a week for a period of two to three months, depending on the results obtained. Four case histories illustrating the favorable results that may be obtained are presented.

Dimercaprol in Pre-Neurological State of Wilson's Disease (Hepatolenticular Degeneration). C. G. Warnock and D. W. Neill. J. Neurol., Neurosurg. & Psychiat. **17**:70-74 (Feb.) 1954.

Warnock and Neill point out that since it was discovered that Wilson's disease (hepatolenticular degeneration) was associated with amino aciduria and disturbances in the copper metabolism, dimercaprol (BAL) has been used in a number of cases in which the characteristic nervous symptoms were already established. When given in appropriate dosage and at regular intervals, dimercaprol caused lessening of tremor and rigidity with consequent improvement in motor function. Whether this measure of control can be maintained indefinitely in long-established cases remains to be seen. The purpose of the paper is to put on record a case in which this treatment was given before the onset of nervous symptoms. The patient, a boy aged 16, is the only surviving and youngest member of a family of three children whose clinical history was described by Warnock in 1952. The first child, a girl, died at age 11 from acute liver failure with jaundice and ascites. The second child, a boy, died at age 21, after a prolonged illness that began with ascites at 9 years and was followed by neurological abnormalities first noticed at age 14 and eventually ending in gross extrapyramidal motor disorder, with contractures, dysphagia, and complete anarthria. The patient, whose case is reported, appeared normal at birth (in 1937), but at age 3 his liver was enlarged and tender and for almost a year before this he had been having frequent loose stools with occasional passage of blood and mucus. Throughout his childhood he had anorexia, pasty complexion, fluctuation in weight, and occasional pyrexia. In March, 1948, at age 10 years and 8 months, faint Kayser-Fleischer rings were seen in both corneae. One month later there were signs of ascites, edema of the lower extremities, and jaundice. There was laboratory evidence of liver dysfunction and a hypochromic microcytic anemia with relative lymphocytosis. Ascites disappeared in four weeks. A dietetic regimen (high protein and carbohydrate, minimal fat) was instituted in May, 1948, and was supplemented with Vitamins A, B complex, C, and K, as well as weekly injections of vitamin B_{12} (200 mcg.). After a year of this therapy, laboratory tests still showed considerable derangement of liver function. Investigations of the copper metabolism were carried out from January to March, 1949. Serum copper levels ranged from 165 to 296 mcg. per 100 ml. in a series of 10 estimations, with a mean value of 200 mcg. per 100 ml. (Normal values are said to range between 86 and 161 mcg.) Urinary copper concentration, in a series of eight estimations during the same period, varied from 22 to 32 mcg. per 100 ml. (normal, 0 to 14.7 mcg. per 100 ml.). A single trial dose of dimercaprol (200 mg.) raised the copper excretion from 253 mcg. to 400 mcg. in the succeeding 24 hours, while the serum copper was elevated from 180 mcg. per 100 ml. before dimercaprol to 280 mcg. per 100 ml. 24 hours later. From May, 1949, onward, repeated courses of dimercaprol were given, and for the past year this has been done at intervals of three months. The dosage used was 400 mg. intramuscularly at four hour intervals on the first day, then at 12 hour intervals for three days, and then once daily for a further four to six days. After four years of treatment with dimercaprol, almost all evidence of hepatic dysfunction had disappeared and nervous symptoms were still absent. The exact significance of copper metabolism in the pathogenesis of Wilson's disease is still imperfectly understood, but it is clear that, in certain cases, elimination of the metal in large quantities, as provoked by dimercaprol, has been beneficial and that the ensuing clinical improvement was not coincidental.

GYNECOLOGY & OBSTETRICS

Diabetes Mellitus and Pregnancy. W. N. Long, W. L. Hartmann, P. H. Futcher and N. J. Eastman. Obst. & Gynec. 3:160-168 (Feb.) 1954.

One hundred eighteen pregnancies that resulted in viable infants were followed in 96 diabetic women in the Johns Hopkins Hospital from Jan. 1, 1942, to Dec. 31, 1952, and were analyzed. With a single exception, all 96 patients had two or more fasting blood sugar levels above 130 mg. per 100 cc. of blood. By improved diabetic control (with a daily diet of 175 to 225 gm. of carbohydrate, 100 gm. of protein, and the balance of calories as fat), together with the increased use of cesarean section before the end of the 38th week, substantial improvement in maternal and infant outcome was achieved. No endocrine therapy was employed in 115 of these pregnancies. There was one maternal death. Of the 118 pregnancies, 62 were followed from Jan. 1, 1942, to June 30, 1948; these resulted in 22 fetal and neonatal deaths, an uncorrected infant loss of 36%. The remaining 56 pregnancies followed from July 1, 1948, to Dec. 31, 1952, resulted in 10 fetal and neonatal deaths, an uncorrected infant loss of 18%. The authors feel that by rigid application of the two principle criteria, i. e., by increased efforts at maintaining the maternal blood sugar within the normal range and by more frequent use of early delivery, often by cesarean section, 12 of the 22 infant losses in the course of the first observation period and 7 of the 10 infant losses in the second period, thus 19 of 32 deaths, or 59%, for the entire 11 year period, could have been prevented. This statement is based in part on the admittedly uncertain premise that a mild to moderate degree of maternal acidosis contributes significantly to late fetal death in utero. While the authors' figures are small, they are at least indicative that a nonpreventable infant loss of 5.5%, which would have been ideally possible, should be set as a goal. Whether it will be possible to achieve such success without the aid of adjuvant endocrine therapy remains to be proved.

Preliminary Experience in Treatment of Menopause with TACE, A New Type of Estrogen. J. S. Gillam, G. W. Hunter and C. B. Darner. J. Clin. Endocrinol. 14:272-277 (March) 1954.

The synthetic estrogen chlorotrianisene (TACE) was used by Gillam and associates for menopausal symptoms in 53 women ranging in age from 27 to 54 years. Ten of the 27 who were undergoing a natural menopause, 6 of 21 who had a surgically induced menopause and 2 of 5 in whom menopausal symptoms resulted from irradiation for cervical carcinoma had received some other form of estrogen before treatment with chlorotrianisene was started. A 12 mg. capsule of the drug in oil was administered twice daily for the first two weeks and once daily for the last two weeks, making a total of 42 capsules (504 mg.) of the drug. Following this, therapy was discontinued until such time as the patient was reevaluated either on a return visit or by questionnaire. Subsequently additional courses were administered. Forty-nine of the 51 patients complaining of hot flushes were completely relieved of this symptom. The side-effects were few. In 3 of the 18 patients who previously had received other hormone therapy the effectiveness of chlorotrianisene was equal to that of the other hormones, and in 15 it was superior. In no instance was this drug less effective than other estrogens. The authors recommend a further trial and more thorough evaluation of chlorotrianisene.

Use of Thyroid Extract in Treatment of Hyperplasia Endometrii. J. W. Ross. J. Nat. M. A. 46:105-106 (March) 1954.

According to Ross hyperplasia of the endometrium occurs from puberty to beyond the menopause, and abnormal uterine bleeding is its most outstanding symptom. Other symptoms are cold extremities, dry skin, brittleness of the nails, breaking-off of the hair, loss of energy, fatigue, low blood pressure, slow pulse, costive bowels, leukorrhea, low basal metabolic rate, elevated serum cholesterol, and sterility. This latter train of symptoms is indicative of hypothyroid activity. Since endocrine imbalance plays a part in the etiology, endocrine therapy seems the logical therapeutic approach. Not satisfied with the results obtained with progesterone, chorionic gonadotropin, testosterone, pregnant mare's serum, and estrogen, the author administered thyroid extract. From 3 to 5 grains (0.2 to 0.32 gm.) were given daily in divided doses. This dosage was continued for 30 days, whether or not the bleeding continued. Three or four, rarely more, such courses were necessary to check the arrhythmic bleeding. During the past five years, 60 cases have been thus treated with gratifying results. The abnormal bleeding was always controlled and the other symptoms were mitigated. There were no alarming side-effects. When the pulse rate was 100 or more or nervousness and diarrhea developed, treatment with thyroid was either temporarily interrupted or reduced. The author feels that the dosages employed in his patients are necessary for the success of this treatment, which increases the metabolism, stimulates the other endocrine glands, hastens the elimination of estrogen from the body, prevents the accumulation of estrogen in the endometrium, and regularizes ovarian (endocrine) disharmony. The author is confident that wider use of this method will establish it as the method of choice in the conservative treatment of endometrial hyperplasia.

Treatment of Cervical Erosion by a Simple Method of Electrocoagulation. E. A. Graber and J. J. O'Rourke. Am. J. Obst. & Gynec. 67:639-646 (March) 1954.

In 100 women with cervical erosion, mild coagulation of the vaginal aspect of the eroded uterine cervix was carried out with a bipolar coagulator consisting essentially of a metal ball split in the middle, with an insulator between, and specially devised for a small portable spark-gap diathermy apparatus. The coagulating ball was placed against the area of the cervix to be coagulated and the current was turned on by means of the foot switch. The current was applied until a whitish-gray area appeared and then was immediately cut off. Using this technique, the entire vaginal surface of the erosion was coagulated. It is better to use a little less current for a slightly longer period, than high current for a short time. It is much safer to undercoagulate rather than overcoagulate. Thirty-four patients had small erosions, 45 medium erosions, and 21 large erosions. Treatment was repeated two to eight times at two week intervals. It was successful in 99 patients, and only in one patient was it a therapeutic failure. Hemorrhages occurred in two patients after the second treatment. A vaginal pack sufficed to control the bleeding, and the erosion healed completely a short time later. In neither case was the bleeding excessive. Coagulation should not be used too near the postpartum period, during the acute stages of cervicitis, salpingitis, or parametritis, or unless smear or biopsy has been taken in any case in which there is a question of malignancy. Except for these contraindications, coagulation is a safe, effective, and simple way to treat erosions of the cervix.

Pruritus Vulvae. W. H. Vogt Jr. Missouri Med. 51:187-188 (March) 1954.

Vogt classifies the causes of vulval pruritus into four main groups and each of these into several subgroups. If vaginal discharge is the cause, this in turn may be due to trichomoniasis, moniliasis, cervicitis, foreign bodies such as pessaries or retained tampons, gonorrhea, or senile changes. Local diseases of the vulva constitute the second group of causes; conditions such as diabetes mellitus or pregnancy the third group; and psychoneurosis, resulting from unsatisfactory sexual adjustment, masturbation, etc. the fourth group of causes. Eradication of the trichomonads by such measures as vaginal acidification plus the use of trichomonacides not only will ordinarily clear the infestation but relieve the itching as well. Applications of gentian violet will often be sufficient to relieve the patient with monilia infestation. If pruritus is attributable to erosions or endocervical inflammations, cauterization of the cervix will often dispense with the discharge and relieve the itching. The use of estrone suppositories in senile vaginal inflammations, of penicillin in gonorrhea, and the removal of irritating foreign bodies followed by one or two cleansing douches will relieve pruritus. Treatment is most difficult in patients in whom no specific causal factor can be identified, and in whom psychogenic factors play a part. These women often go from general practitioner to dermatologist, to radiologist, to gynecologist,

to surgeon, in about that order. Treatments of all types such as x-rays, crude tar, antihistamines, fatty acids, alcohol injections, vulvectomies and all sorts of lotions, salves, and local anesthetic ointments have been recommended in the recent literature. The author feels that in these cases an attempt should be made to relieve the patient's mind, perhaps by helping to solve family problems. The demand to cease scratching should be repeated. At night an antipruritic ointment containing 5% crude coal tar, 5% zinc oxide, 45% starch, and 45% soft paraffin can be used. This greenish black paste serves to relieve the itching and indicates whether the patient has scratched during the night. Mild sedation with phenobarbital promotes sleep and reduces itching. If x-ray treatment has not been used previously three or four applications of 75 to 100 r are often helpful. The need for local treatment in a trouble largely originating in the mind is due to the fact that scratching produces thickening of the epithelium, while crude tar applications and x-ray treatments give relief by decreasing local susceptibility to the itching stimuli.

Hemangiopericytoma of the Uterus. P. Pedowitz, L. B. Felmus and D. G. Grayzel. Am. J. Obst. & Gynec. **67**:549-563 (March) 1954.

Reexamination of specimens of tumors previously diagnosed as sarcoma or hemangioendothelioma revealed four hemangiopericytomas. The only presenting symptom common to the four patients who were between the ages of 25 and 77 years was vaginal bleeding. This was probably due to the proximity of the neoplasms to the endometrial cavity. Recurrence of the tumor was noted in two cases, one with invasion and one with metastasis. These were the only evidences of malignancy observed. Except for metastases, the benign or malignant character of the neoplasm can be determined only by its future clinical course. Postoperative radiation therapy was given to the four patients. Three were alive and well 6, 8, and 11 years after hysterectomy despite a local recurrence of the tumor in one patient. The fourth patient died 18 months after the diagnosis was first made and 4½ years after the appearance of postmenopausal bleeding. The basically vascular cytoarchitecture of the tumor, the essential component of which is pericytes radially arranged around proliferating capillaries, can be demonstrated only by the utilization of differential stains. Silver stains demonstrate not only fine reticulum sheaths of capillaries but also occult and compressed vessels. Although hemangiopericytoma is a relatively rare type of vascular neoplasm of the uterus, differential staining af all vascular neoplasms would undoubtedly increase the number of such tumors detected. Tumors of the uterus, previously reported as "stromal myosis" are probably identical with hemangiopericytoma and should be so designated.

Carbohydrate Metabolism During Pregnancy. J. P. Hoet. Diabetes **3**:1-12 (Jan.-Feb.) 1954.

In women with a diabetic trait or with latent weakness of insulin production, pregnancies disturb the regulation of the carbohydrate metabolism, as evidenced by the hyperglycemic tolerance curve. This curve does not become abnormal until after the fourth month of pregnancy, and there may be no glycosuria. This disturbance in regulation disappears or diminishes after delivery. The consequences to the fetus are serious. The fetal loss rate increases from 20 to 50% in proportion to the increasing severity of the disordered glucose metabolism. A large number of the infants who are born alive have an excessive weight. The hyperglycemic or prediabetic dysfunction provokes hyperplasia of the islands in infants born of diabetic mothers. The tendency to obesity, hyperglycemia, and finally diabetes that characterizes the ultimate development of a great number of these infants are the consequence, on the one hand, of heredity and, on the other hand, of the maternal environment or "milieu interieur" during embryonal development. The correction of these disturbances of carbohydrate metabolism by insulin reduces the fetal loss rate and the infant mortality. One may anticipate that by normalizing the maternal environment, the hyperplasia of the islands will be reduced. The second part of this paper reviews experimental studies, such as pregnancy in animals in which the pancreas has been damaged by alloxan; the abortifacient action of cortisone; and the influence of cortisone on placental glycogen. The author feels that these experimental studies give hope that by correcting the transitory hyperglycemia of pregnancy by means of insulin, the newborn of so-called prediabetic mothers will not only survive but will have normal growth and development. In order to recognize prediabetic mothers it is necessary to perform sugar tolerance tests in each trimester of pregnancy, especially in women of families with a tendency to diabetes. Observations on the differences between children of diabetic mothers and diabetic fathers point to the causative importance of the maternal environment. The correction of the hyperglycemia of pregnancy by insulin may prevent the appearance of diabetes in the mother and the anatomic and functional anomalies due to diabetic embryopathy in the infant.

PEDIATRICS

Pathogenesis of Mongolism Following Maternal Illness: Role of Adrenals. E. E. Brown. Arch. Pediat. **71**:47-53 (Feb.) 1954.

Brown shows that many theories of the causation of mongolism are not tenable. His own investigations at first suggested that advanced age of the mother seemed to be a factor. Further analysis of his cases revealed illness of the mother during early pregnancy, in part caused by chronic infections such as sinusitis, nephritis, bronchitis, bacterial asthma, and rheumatic pains. The "target hypothesis" best explains the mechanism by which maternal illness during early pregnancy is followed by the birth of a mongol. The target may be the embryonic adrenal cortex, as inferred from its organogenetic role, from the experimental effect of cortisone on the embryo of pregnant animals, and from the presence in mongols of numerous hypoadrenic symptoms. The pathogenic agent may be some type of infection (virus, toxin), anoxia, or ionized air, any of which might affect the adrenal cortex of the embryo. Presumably when the adrenals are rendered defective by the toxic agent, organogenesis is delayed, retarding most seriously the development of the brain, but there also may be incomplete closure of cardiac septums and other defects, such as hernia, epicanthus, hypoplastic gonads, chimpanzee-like ear, and simian palmar line. Ontogenesis being retarded, "atavism" results. The term atavism is used descriptively and without hereditary implication. The simian appearance including chimpanzee lip and chimpanzee-like ear, Darwin's tubercles, peculiar posture of head seen in apes, wide separation of the big toe from remaining toes, transverse fold across the whole palm similar to the one found in anthropoid apes, myopia, duplicated nipples, the smaller skull and brain, the glance from below upwards, and wry position of the head all suggest atavism.

Vomiting and Diarrhea with Fatal Circulatory Collapse in Children Following Treatment with Chloromycetin and Terramycin: Discussion of Staphylococcic Enteritis. R. Cramer and E. Rossi. Helvet. paediat. acta **8**:544-560 (Dec.) 1953. (In German.)

Cramer and Rossi point out that the fatalities resulting from antibiotics have usually been due to anaphylactoid reaction, Jarisch-Herxheimer reaction (in the course of the treatment of syphilis or of typhoid); fatal damage to hematopoiesis by chloramphenicol (Chloromycetin); or superinfection, usually generalized moniliasis that often results in leukemia. In the five children whose histories are presented here, uncontrolled vomiting and diarrhea developed from 5 to 10 days after the beginning of treatment with oxytetracycline (Terramycin) and chloramphenicol (Chloromycetin), at a time when the disorders being treated (paratyphoid, atypical pneumonia, and influenzal meningitis) had been greatly improved or practically cured. The vomiting and diarrhea in turn led to fatal circulatory collapse. In two cases a pseudomembranous enteritis due to staphylococci could be demonstrated. This new clinical entity has been de-

scribed in adults as a complication of antibiotic therapy. There is a similarity between this form of enteritis and the clinical pictures of staphylococcic food poisoning. Hematological changes in the blood and bone marrow, particularly the agranulocytosis appearing in one case, are discussed. The treatment of such patients requires in addition to energetic rehydration, the substitution of the new antibiotic erythromycin that has proved effective against staphylococci.

Infantile Cortical Hyperostosis: Inquiry Into the Etiology and Pathogenesis. J. B. Sidbury Jr. and J. B. Sidbury. New England J. Med. **250:**309-314 (Feb. 25) 1954.

There are over 60 cases in the literature of the syndrome known as infantile cortical hyperostosis. It is characterized by the usually sudden onset of swelling of the face, thorax, or extremities, hyperirritability, fever, fluctuating course, and roentgenographic evidence of periosteal new bone formation. The authors report 10 new cases and state that the syndrome is probably more frequent than is commonly supposed. The disease begins in the first five months of life; the average age at onset in the cases reported by the authors and those collected from the literature was nine weeks, and two cases were diagnosed in utero. Infection, trauma, allergy, endocrinopathy, maternal causes, birth factors, and dietary aberrations do not appear to be involved in the cause of this hyperostosis, but there is increasing evidence that intrauterine or genetic factors are responsible. Occurrence in siblings and associated congenital anomalies have been reported, though not in so high an incidence as would be expected. From the clinical and microscopic findings, the authors conclude that infantile cortical hyperostosis is a secondary manifestation of a defect of the arterioles supplying the affected areas. On microscopic examination, the arteries of the overlying soft tissues and periosteum showed intimal proliferation, and it is presumed that the resulting hypoxia causes focal necrosis of the overlying soft tissues and a proliferative reaction of the periosteum. Therapy is symptomatic and supportive. Sedation is often indicated for the hyperirritability. An adequate diet with supplementary vitamins and transfusions for the anemia that develops in the majority of the patients are good supportive measures. Hormone therapy with corticotropin and cortisone has been tried in 12 cases and appears to have shortened the course of the illness.

Neurological Sequelae of Tuberculous Meningitis in the Child. H. Danon-Boileau. Encéphale **43:**73-92 (No. 1) 1954. (In French.)

Neurological sequelae, though comparatively rare in tuberculous meningitis, are most frequent and severest in children attacked by the disease during the first three years of life. Hemiplegia of varying intensity, aphasia, deafness, vestibular disturbances, and epilepsy were the principal sequelae found in two groups of patients studied by the author. Hemiplegic sequelae, classified according to the degree of functional incapacity exhibited, were studied in 12 of 263 patients discharged as cured up to May, 1952. Hemiplegia of the first or severe degree, characterized by inability to walk without support or to move the arms except by a few gross movements of the shoulder, was found in two cases. Six patients had disability of the second or moderate degree, in which, though unsupported walking is possible, the gait is abnormal and falls are frequent; the forearm can be bent and extended, partially if not completely; the hand either cannot be used or can be opened only with great difficulty; muscular strength on the affected side is notably diminished; and effort is accompanied by synkinesis. Patients with slight or third degree disability have an almost normal walk, in spite of discrete lameness, and tire easily; their hand movements are clumsy; and their muscular strength is impaired. Sequelae of the fourth degree can usually be detected only on neurological examination. There were two patients in each of these last two classifications. Prognosis depends largely on the character of the sequelae. Improvement can scarcely be expected in patients with severe hemiplegia associated with profound mental retardation; those with moderate disability may improve slowly over a period of years; and in the rest recovery will be practically, if not neurologically, complete. Arteritis of meningoencephalitic origin, the appearance of the condition before the age of 4 or 5 years, and prolongation of the period that elapses before the first signs of recovery are seen, especially for more than 3 or 4 months, all affect the prognosis unfavorably. Familial and personal affective conditions also play an important part in the patient's recovery. Aphasia was unmistakably evident in four children; in all of whom it was associated with hemiplegia on the right side. Disappearance of the aphasic phenomena was complete in three cases, with improvement beginning within from 12 days to 2 months. Recovery from aphasia did not begin in the fourth patient, however, until 10 months after the initial accident, and the final result is still in doubt. Deafness, though less frequent now than formerly, is a severe complication affecting the child's language and character, and every effort should be made to detect it and to institute reeducative procedures as soon as possible. Vestibular disturbances of varying severity were clinically discernible in 47 of 56 children who had had meningitis after the age of 3 years, but even those that were most pronounced at first tended to improve in time. No significant signs of vestibular involvement were found in any of the 16 children who were less than 30 months old when they contracted meningitis. Epileptic sequelae, which occurred in only 10 of the 300 children studied and were associated with mental retardation in 6, responded satisfactorily to the standard methods of treatment.

Hydrocortisone Ointment in the Treatment of Infantile Eczema. V. H. Witten, A. B. Amler, M. B. Sulzberger and A. G. De Sanctis. A. M. A. Am. J. Dis. Child. **87:**298-304 (March) 1954.

Thirty children between the ages of 2 months and 6 years with the infantile form of atopic dermatitis ("infantile eczema") were treated by the "simultaneous paired comparison" method in which a 2.5% hydrocortisone free alcohol ointment (consisting of wool fat U. S. P. 15%, liquid petrolatum, 10% and white petrolatum, 75%, to which hydrocortisone free alcohol was added in concentration of 25 mg. per gram) was applied to the affected areas of the right side of the body, and control ointment consisting of the vehicle without the hydrocortisone free alcohol to the contralaterally affected areas of the left side. Favorable response to the hydrocortisone free alcohol ointment was noted in 18 of the 30 patients. There were no cases in which intolerance to the medication was noted. It was not necessary at any time to discontinue the ointment because of irritation, allergic eczematous contact dermatitis or because of staining of skin or bed linen, odor, or stinging or burning sensations. In no case was a spread of local superimposed infection noted as a result of the repeated and prolonged topical application of the hydrocortisone free alcohol ointment. In nine infants, approximately one-half or more of the body surface was covered with the ointment two to three times a day for one to seven weeks without a single case of clinically evident undesirable effects due to absorption of the hydrocortisone. The authors are of the opinion that the hydrocortisone free alcohol ointment constitutes the simplest, cleanest, and most rapidly effective of all the topical measures they have employed in the treatment of infantile eczema.

The Low Salt Syndrome in Children During Hot Weather. M. E. Evans. J. Kansas M. Soc. **55:**125-129 (March) 1954.

The occurrence of the low salt syndrome as a result of losses of water and sodium chloride by sweating and of inadequate replacement of these losses in hot summer months is described in two boys, aged 14 months and 3½ years, and in a 14-month-old girl. According to weather bureau data, the maximum temperature at the time of the occurrence of the low salt syndrome in these patients varied from 95 F to 102 F and the maximum humidity from 72 to 94%. Children in hot weather sweat, are anoretic, have low grade fevers, vomit, and are sometimes lethargic. Extreme lethargy deepening into coma, with

abnormal neurological signs, opisthotonos, and convulsions, are observed less frequently. The two boys recovered after administration of 18.3 gm. of sodium chloride in 3,200 cc. of various solutions and 8.85 gm. of sodium chloride in 1,600 cc. of fluids, respectively. The baby girl who had been anuric from admission even though 1,500 cc. of fluids had been given orally and intravenously containing 6.63 gm. of sodium chloride became opisthotonic and died 18 hours after admission. Necropsy revealed fibrocystic disease of the pancreas. One of the boys was known to have fibrocystic disease of the pancreas before his illness with the low salt syndrome, while the other apparently did not have this illness. The finding reported by other workers that the sweat of children with fibrocystic disease of the pancreas who were exposed to high temperature associated with high humidity cointained 60 to 160 mEq. per liter of chloride as compared to 4 to 80 mEq. per liter of chloride in those with various other disorders suggests that the results of heat stress in children with fibrocystic disease of the pancreas are much more devastating than in children without this disease. Every child who tolerates heat poorly should be studied carefully with the possibility of fibrocystic disease in mind, and all infants known to have fibrocystic disease of the pancreas should receive extra sodium chloride. The low salt syndrome is not necessarily the inevitable consequence of excessive sweating, but, rather, the inevitable consequence of inadequate replacements of water and electrolyte losses through sweating. Failure to replace these losses is often due to failure to recognize the need for replacement.

Renal Tumors in Childhood. L. S. Scott. Glasgow M. J. **35**:33-45 (Feb). 1954.

Scott reviews observations on 70 children with renal tumors observed at the Royal Hospital for Sick Children, Glasgow, between 1916 and 1952. The patients' ages ranged from 2 months to 12 years. Wilms' tumor (embryoma) existed in 61 of the 70. This is the commonest tumor of the urinary tract in children and occurs in about the same frequency in both sexes. The presenting symptom is generally a palpable swelling discovered accidentally by the child's mother. The classical triad of swelling, pain, and hematuria so commonly found in renal tumors in adults is rare in children with Wilms' tumor. A palpable swelling was present in 60 of the 61 children, and it was the first symptom in 28. Abdominal pain, not renal in type, was present in 18 and was the first symptom in 12. Hematuria was present in 13 and was the presenting symptom in 12 of these. The classical triad was present in only six, and in nine the onset was silent, i. e., symptoms referable to the renal tract were absent, the tumor being discovered during investigation for general debility. Intravenous pyelography, which is carried out routinely at the author's clinic, fulfills the double purpose of demonstrating the presence of the contralateral kidney and, at the same time, helping to differentiate the lesion from sympathicoblastoma, hydronephrosis, and polycystic kidney, the three conditions with which embryoma is most likely to be confused. The tumor arises within the kidney substance, and, as it grows, it expands the renal capsule that surrounds the neoplasm for a considerable period of time before rupturing. The histological appearances are so varied that its terminology has included embryoma, nephroblastoma, embryonal sarcoma, rhabdomyosarcoma, chondromyxosarcoma, lipomyosarcoma, etc. Ten of the 61 cases of embryoma are excluded from the statistical analysis, because there was no histological proof of the diagnosis. The fate of 8 of the 51 proved cases is unknown. Of the 43 patients followed up, 35 are known to have died and only 6 can be regarded as having probable "cures" (freedom from recurrence or metastases for two years after operation). Two other children are alive and free from recurrence but have not yet reached the two year "standard" of probable cure. Of the nine children with renal tumors other than embryoma (Wilms' tumor), one had hemangioma of the renal pelvis, one carcinoma, one sarcoma, one teratoma, and five malignant reticuloses, including four cases of lymphosarcoma and one of lymphadenoma. These five cases in which the kidneys were involved in a generalized malignant reticulosis are presented in some detail, and Scott points out that many authors support the view that the term Hodgkin's disease should be replaced by lymphosarcomatosis. He himself is of the opinion that the term malignant reticulosis covers the histological variants.

Report of Seven Cases of Chondro-Osteo-Dystrophy (Morquio's Disease). W. F. Townsend-Coles. Arch. Dis. Childhood **29**:7-11 (Feb.) 1954.

Townsend-Coles presents the histories of seven cases of eccentro-osteochondrodysplasia (Morquio's disease) occurring in three sets of siblings in northern Sudanese families. In each set the parents were close blood relatives, but all appeared healthy. The affected children were said to have been healthy at birth and to have remained so until the seventh or eighth month when deformity appeared. Dwarfing and deformity became more evident with increasing age. The normal development of the head made it appear large by comparison with the stunted trunk and limbs, and the excessive shortening of the trunk gave the arms a false appearance of length. The deformities included shortness of the neck, anteroposterior enlargement of the chest, eversion of the costal margin, pointing of the sternum, and dorsolumbar kyphosis. The limb bones were short but enlarged at the ends giving the joints a swollen appearance. The large olecranon processes prevented full extension of the elbows, and there was ulnar deviation of the hands at the wrist joints. Genu valgum and partial flexion of the knee joints were present, and the feet were short, wide, flat, and everted at the ankle. Marked laxity of the muscles and ligaments allowed the joints undue mobility. Roentgenologic studies revealed that the vertebrae were flat, irregular, and poorly calcified. The anteroposterior diameter of the pelvic brim exceeded the transverse (ape pelvis), and the acetabular roofs were irregular. The ends of the ribs were abnormally wide. The long bones were short, thick, and poorly calcified. One of the two deformed children in the first family was 21 years old. With a height of 34.5 in. (87.63 cm.) and a weight of 41 lb. (18.6 kg.), she was a severely crippled and deformed dwarf who could neither stand nor walk. Her brother, also a deformed dwarf died at the age of 14. The two deformed children in the second family were both girls. Of the three deformed children in the third family, one was a boy and two were girls. The father of these children had a second wife of whom he was not a blood relation. None of their seven children were deformed. Morquio's disease is usually regarded as being transmitted as a Mendelian recessive and the patients described here, being of both sexes and the offspring of closely related parents, conform to this view.

DERMATOLOGY

Nodular Granulomatous Perifolliculitis of the Legs Caused by Trichophyton Rubrum. J. W. Wilson, O. A. Plunkett and A. Gregersen. A. M. A. Arch. Dermat. & Syph. **69**:258-277 (March) 1954.

In California during the two years preceding the writing of the paper, 14 cases were discovered in which nodules composed of a chronic granulomatous infiltrate surrounding infected hair follicles were prominently displayed within the confines of plaques of scaly erythematous trichophytosis usually distributed unilaterally on the lower portions of the legs of dark-haired women. Trichophyton rubrum (purpureum) was uniformly recovered in culture from material removed superficially from the areas of dermatophytosis as well as from the sides of the deeper portions of specimens removed for biopsy. Histopathological preparations stained by the Hotchkiss-McManus method revealed fungus elements in hair shafts as well as in the midst of chronic granulomatous areas in the corium. Clinically and histopathologically, the process closely resembles Majocchi's trichophytic granuloma in many respects. The location and distribution of the disease and the causative organism are different, however, as is the tendency to unilaterality.

Therapy has been successful in controlling the disease in most instances, using potassium iodide orally, mildly filtered x-radiation locally, and topical applications of Asterol dihydrochloride (6-[β-diethylaminoethoxyl]2-dimethylaminobenzothiazole) as a fungicide, in both tincture and ointment form. Recurrence is to be expected in many instances because foci of trichophytosis remain uncured in nails, soles, or other areas, and there are unknown factors in the pathogenesis and epidemiology of T. rubrum infections, rendering certain persons abnormally susceptible.

Vesicular Lesions of Skin in Cases of Coma. C. W. Olsen. J. Nerv. & Ment. Dis. **118**:412-415 (Nov.) 1953.

Olsen points out that, when vesicular lesions of the skin develop in unconscious patients, the possibility of thermal burns is naturally considered, and in cases such as intoxication, asphyxiation, and anesthesia or deep sedation suspicion of negligence may arise. In acutely ill patients who are unconscious, an unusual susceptibility to breaking down of the skin in pressure areas is sometimes said to be the result of nerve injuries. This theory cannot be refuted. In coma there is unrelieved pressure on the skin due to immobility. Furthermore, respiration and circulation are depressed, and in some cases residual neuritis is found after the patient regains consciousness. Blisters resulting from pressure are second degree decubitus lesions, which in the terminology of burns fall between erythema (wheals or welts) and deep necrosis. In the same patient in whom blisters are found, the surface of skin may also show wheals and ulcers, but the vesicles and bullae most strongly suggest burns such as may be attributed to heating pads, hot water bottles, moist heat applications, infra-red light therapy, or diathermy. The author cites several case histories to illustrate that the nature of vesicular lesions developing during coma and the responsibility for their occurrence may assume medicolegal interest. He emphasizes that they are "second degree" decubitus lesions. They are not pathognomonic of any one kind of coma, but are seen in carbon monoxide poisoning, asphyxia with natural gas, barbiturate intoxication, and spinal anesthesia.

Moniliasis of Oral Mucous Membrane. J. Meyer-Rohn. Hautarzt. **5**:112-115 (March) 1954. (In German.)

The occurrence of moniliasis of the tongue and of the hard palate is described in a 51-year-old woman. Greasy ulcers, with a whitish coat, very tender to touch, were present for 32 months at the tip of the tongue, at the soft and hard palate, and on the mucosa of the vestibule of the mouth. The condition was kept stationary with local application of various disinfectants and administration of 3,600,000 units of penicillin. Some of the ulcers were removed by curet with the aid of hexobarbital sodium anesthesia. Repeated smears of the floor of these ulcers revealed profuse growth of Candida albicans. The bacteriological diagnosis of C. albicans was established by sugar fermentation tests. Fermentation of dextrose, levulose, and maltose was produced, but fermentation of saccharose and and lactose did not occur. The causative role of C. albicans was demonstrated by the hemagglutination between the serum of a rabbit (which had been infected with the strain obtained from the patient) and the erythrocytes of the patient. Temporary improvement was obtained with local application of 25% glycerin borax and a pyrazol derivative combined with oral administration of 60 gm. of a proprietary sulfonamide compound. Best results were obtained with daily local applications of malachite green for eight weeks, combined with quartz lamp irradiation and administration of tonics. The clinical aspect and the bacteriological and serologic findings justified the diagnosis of moniliasis. Prognosis for cure is unfavorable, and prognosis for survival is doubtful. There is no effective chemotherapy available for moniliasis. Ingestion of food will be difficult temporarily and will lead to loss of weight and strength and consequently to increased tendency to infection. Fatal invasion of the circulation must be expected eventually.

UROLOGY

Management of Ureteral Calculi. A. K. Doss. J. Louisiana M. Soc. **106**:47-51 (Feb.) 1954.

According to Doss, excretion urograms are of inestimable value in determining the course of management of ureteral calculi to be pursued. If the degree of obstruction is minimal or absent one may temporize. If the amount of obstruction is pronounced to complete, relief from the obstruction either by passage of ureteral catheters by the point of obstruction with fixation of the same in place to initiate drainage or actual removal of the calculus becomes mandatory. In the presence of a high degree of obstruction, it is necessary to decompress the obstructed kidney if renal damage is to be prevented. This may be done either by removal of the stone or by tying in ureteral catheters that have been passed beyond the point of obstruction. In general, calculi confined to the upper half of the ureter, requiring prompt attention, may be removed through a small muscle-splitting incision placed so as to come down directly on the point of ureteral obstruction. With the muscle-splitting procedure, convalescence is reduced to a bare minimum complicated only by rather free drainage of urine from the operative site until the incised ureter has had opportunity to seal over, usually requiring four to five days. Calculi located in the lower half of the ureter, and more especially in the lower third, may be with a rare exception removed through manipulative effort. After removal of the calculus, two no. 5 catheters are tied in the ureter together with a Foley bag catheter in the bladder to which the ureteral catheters are anchored. These are allowed to remain in place several days so that ureteral edema may subside before their removal. If a high degree of obstruction persists after an unsuccessful attempt at manipulation and if it is impossible to establish drainage by passing the point of obstruction with a ureteral catheter, then ureterotomy should be done promptly. Failure to employ immediate surgical intervention may result in loss of a kidney or even in death. Success with the so-called antispasmodic drugs in an attempt at assisting passage of ureteral calculi was not impressive in the author's experience. Manipulation of a calculus may result in ureteral perforation that need not cause much concern. Exploration and drainage of the perforated site is only occasionally necessary. It is well for all patients who have had ureteral calculi removed to have an excretion urogram made within six weeks to three months after the attempt. Similar observations over a long period may also be in order.

Radical Retropubic Prostatectomy for Cancer. R. Chute. J. Urol. **71**:347-372 (March) 1954.

Carcinoma of the prostate is surprisingly common, the average of the figures of four independent investigators giving an incidence of 24% in a large series of routine autopsies in men 50 years of age or over. Most of these carcinomas were small and had not spread beyond gland nor been the cause of death. Carcinoma of the prostate is usually a slow-growing tumor, when it is still confined inside its capsule, where it can be detected by rectal palpation. When it escapes from the capsule, it spreads and metastasizes. Despite the favorable results of radical surgery in cases detected in the early stage, the cure rate of cancer of the prostate is low for two reasons. 1. In the majority of cases, the disease progresses so silently that, by the time it causes symptoms bothersome enough to lead the patient to consult a physician, it has already spread and become inoperable and possibly has also metastasized. The only defense against this is an educational program for an annual rectal examination of all men over 50. 2. Although radical perineal prostatectomy, in early cases, has produced results superior to those of hormonal therapy, which is palliative only, nevertheless most urologists will not perform this operation. Because an error in technique may result in incontinence or a rectourethral fistula, they prefer riskless hormonal therapy, with transurethral resection as necessary, which usually will give a few years of palliation. As an antidote for this bad situation, radical retropubic prostatectomy has been developed. This operation gives results just as good as the radical perineal procedure as regards

the cure of cancer, carries no greater mortality, is easier to perform, and is associated with less danger of rectal fistulas. Postoperative incontinence is about the same as after the radical perineal method. Osteitis pubis is rare. Abdominal exploration or dissection of pelvic nodes, both impossible via the perineal approach, can be carried out during the retropubic operation. The injection of radioactive gold, if extraprostatic spread is found, can be done in conjunction with it.

OPHTHALMOLOGY

Intramuscular Chloramphenicol Treatment of Trachoma. J. B. Chastain and L. K. Newlin. Rocky Mountain M. J. **51:**191-194 (March) 1954.

Chastain and Newlin feel that in the western states, at least, trachoma should be considered in the differential diagnosis of ocular infections, regardless of race or occupation. They evaluate the intramuscular injection of chloramphenicol in the treatment of active trachoma. They resorted to this treatment for the following reasons. 1. The sulfonamides and antibiotics commonly used are at times ineffective or allergenic. 2. A shorter treatment for trachoma is desirable. 3. Parenteral therapy is more desirable than oral therapy in the population groups in which trachoma is most prevalent. A special suspension of chloramphenicol was used. Crystal size was controlled in order to assure ready suspension, easy administration, and relatively uniform absorption. An inert dispersing agent has been added to the formula to speed up the suspending process. One gram of chloramphenicol is contained in 2.5 cc. of the suspension. Twenty-five patients having late stage 2 or stage 3 trachoma were successfully treated with daily intramuscular injections of 1 gm. of chloramphenicol. There was no additional local medication of any type. Patients treated with chloramphenicol parenteral suspension were improved in an average of nine days. There were no significant blood or urinary changes, also no allergic reactions. There was no evidence of local reaction at the site of injection. Twenty-six patients received a combination of sulfadiazine orally and sodium sulfacetamide ophthalmic ointment, 10%, locally. Twenty-two patients responded favorably to sulfonamide therapy. Two patients who failed to respond to the sulfadiazine-sodium sulfacetamide combination, one patient who relapsed following treatment with sulfonamides, and one patient who was allergic to the drug all responded to chloramphenicol injections. Chloramphenicol therapy should be continued until the pannus has lost its injection and appears moderately gray in color.

Further Experiences of Intra-Ocular Acrylic Lens Surgery with Report of More than 100 Cases. H. Ridley. Brit. J. Ophth. **38:**156-162 (March) 1954.

Satisfactory acrylic lenses for intraocular implantation have been available since March, 1951, and they have been used since then in 150 operations. It is now known that the artificial lens of standard design composed of Transpex and correctly inserted in an eye is well tolerated for several years. It is not known whether any degenerative changes will be found either in the patient's eye or in the acrylic lens in 10 years or in 50 years, but at the present there is nothing to suggest future trouble. On the contrary, the longer the lens has been in place the better it appears to be tolerated. The combination of intracapsular extraction and insertion of an acrylic lens proved unsatisfactory. Deliberate intracapsular technique was employed in 10 cases in which the cataract was largely confined to the nucleus or the posterior cortex. It proved possible to slide the acrylic lens over the unbroken vitreous face and to set it in position behind a central and circular pupil, a procedure that requires exceptional care and more than average risk. The intraocular acrylic lens was inserted perfectly in all 10 eyes undergoing deliberate intracapsular extraction, but in 7 it underwent spontaneous dislocation into the base of the vitreous chamber. This misfortune occurred not immediately, but several months after operation, in some instances in association with attacks of coughing. Since only three cases remain satisfactory, the intracapsular technique is contraindicated. In eight other cases in which extracapsular extraction had been planned, the posterior capsule had been removed accidentally, and these, therefore, became "inadvertent intracapsulars." Dislocation resulted in three of these cases. Insertion of an intraocular acrylic lens after extracapsular extraction is the only method now employed, and where the posterior lens capsule has not been damaged there has been no dislocation of the lens in the absence of trauma. When intraocular acrylic lens surgery was first started it was feared that the posterior capsule might thicken and that "secondary cataract" might cause visual deterioration some time after operation. It was hoped, however, that the pressure of the the lens on this very thin membrane would prevent wrinkling and thickening, and this, in fact, has been the experience so far. The author feels that time has yet to show whether in cases of bilateral cataract the optical, cosmetic, and psychological advantages outweigh the disadvantages of extra complication and slower recovery of sight compared with the classical technique; but there is evidence, in the scores of good results and the general absence of severe complications, that in years to come the acrylic lens may be the operation of choice for all cataracts that are uncomplicated by severe ocular or constitutional disease.

THERAPEUTICS

Antibacterial Synergy of Tyrothricin, Bacitracin and Cobalt. P. V. Forni and A. Ruggenini. Arch. sc. med. **79:**82-103 (Jan.) 1954. (In Italian.)

Studies were made to evaluate the synergy of tyrothricin with bacitracin, of each of these antibiotics with cobalt, and of the three antibacterial factors combined. The standard serial dilution technique was followed, and strains of Micrococcus (Staphylococcus) aureus of Oxford and Escherichia coli grown on agar culture were used. A synergistic effect was found between bacitracin and tyrothricin on both M. aureus and Esch. coli. Various hypotheses have been advanced in the past to explain this synergy; the most reliable seems to be the one that considers the two preparations capable of influencing two different enzymatic phases of the bacterial cell metabolism; in this way a greater growth inhibition is obtained than would be secured with the alteration of only one of these phases. There is synergy, however, only when the two preparations are administered simultaneously. Cobalt potentiated the antibacterial activity of both antibiotics. Its potentiating action was more evident with bacitracin for bacteriostatic activity and with tyrothricin for bactericidal activity. When the three factors were combined, the antibacterial activity was greater than that of each antibiotic alone, of the two antibiotics combined, and of each antibiotic combined with the metal. Within 30 minutes the plates were completely sterile. The mechanism of action in this last experiment is attributed to a cobalt-induced sensitization of the bacterial cell to the antibiotics: because of the well-known activity of the metal for protein substances, this sensitization may be explained by the formation of some combinations of the cobalt with the cytoplasm proteins.

Long-Term Antibiotic Therapy in Chronic Bronchitis and Infectious Asthma: Control and Prevention of Bronchopulmonary Disease. W. Finke. Antibiotics & Chemother. **4:**319-329 (March) 1954.

Seven years ago Finke began a study in which about 400 patients with bronchopulmonary infection underwent prolonged antibiotic therapy. He presents observations on 135 adults and 109 children (under 16) who were treated and followed-up for over a year (average 33 months). Of the adults, 54 had early or moderately advanced cases and 81 far advanced cases. Bronchographic studies in 85 patients revealed 36 instances of definite and 20 of probable bronchiectasis. Chronic emphysema was present in 64 patients. In most of the 109 children, the characteristic syndrome of an incipient or established bronchopulmonary disease—persistent cough and recurrent, major respiratory infections—had its onset before the age of 2, and 37 had a history of one or more episodes of pneumonia. Forty-six children had undergone tonsillectomy and adenoidectomy, and in 48 obstructive bronchitis causing wheezy dyspnea had led to a diagnosis of allergic bronchial asthma. True respiratory

allergy was absent in cases of this group or, if present, played a lesser role than did infection. Eighty-four children could be considered as having early or moderately advanced cases and 25 as having advanced. Roentgenographic studies showed in nearly half of them lesions, such as incompletely resolved pneumonia, patchy atelectasis, fibrosis, and emphysema, and the remaining usually presented heavy hilus and increased bronchovascular markings. Bronchographies were done in 31 instances and revealed 5 definite and 9 probable cases of bronchiectasis. Penicillin was used as the main form of treatment, the parenteral route being replaced more and more by oral and aerosol therapy. The daily oral dose of penicillin taken on an empty stomach varied between 1,000,000 and 3,000,000 units in the beginning, and 500,000 to 1,000,000 units later on; dosage was determined more by the severity of the disorder than by the patient's age. Penicillin aerosol, which provides high local concentration, was given to most adults and older children. Two hundred thousand to 500,000 units of crystalline powder or soluble tablets, dissolved in from 1 to 2 cc. of a nonirritating detergent, were inhaled one to three times a day. Finke says that the results obtained with long-term antibiotic therapy dispel false hopes, but also contradict skepticism and exaggerated fears. The younger the patient and the more recent and the less severe the disease, the greater the probability for full recovery. A dramatic early improvement, probably due to elimination of a superimposed infection, rarely signified quick recovery from the chronic infection. In most chronic cases, respiratory symptoms reappeared within six months after discontinuation of therapy, but even these short remissions, and the response to subsequent treatment, meant rehabilitation for otherwise hopeless cases. In earlier cases, especially in children, an active therapeutic approach was more promising than the hope of outgrowing the condition. The parenteral administration of penicillin and large oral doses of broad spectrum antibiotics caused serious complications in some patients who had tolerated oral and aerosol penicillin prior to their shock reaction from the parenteral administration and continued to tolerate them afterward.

Relation of Dietary Protein Levels to Pancreatic Damage in the Rat. M. Wachstein and E. Meisel. Proc. Soc. Exper. Biol. & Med. **85**:314-317 (Feb.) 1954.

Wachstein and Meisel observed the development of atrophic lesions of the pancreas in rats eating a completely protein-free diet. Supplementation of such a diet with 2% casein is without influence on the pancreas, while either 4% casein or 1% methionine have a marked beneficial effect. With a synthetic diet containing 7.5% casein, the microscopic appearance of the pancreas is almost normal.

Pharmacological Aspects of Barbiturate Intoxication. E. J. Wayne. J. Forensic Med. **1**:172-174 (Jan.-March) 1954.

The barbiturates depress the central nervous system with little effect on the circulation or metabolism, but with a pronounced tendency to cause respiratory depression. It is dangerous to use the short-acting barbiturates in liver disease and the long-acting barbiturates in renal disease. One aspect of the action of barbiturates that is of special importance is that alcohol potentiates their action and that both the lethal dose and the anesthetic dose of a barbiturate are less if alcohol is present in the blood and tissues. Morphine also potentiates the action of barbiturates on the respiratory center. Another point to which Wayne draws attention is the great variation in the dose of a barbiturate required to induce anesthesia. The mean narcotic dose of amobarbitol (Amytal) sodium is about 11 mg. per kilogram, but the range is from 4 to 18 mg. per kilogram. With most barbiturates there is, in a group of 100 persons, at least a fourfold difference between the dose required to give the same effect in the least and the most susceptible person. The common symptoms of acute barbiturate poisoning are drowsiness and confusion progressing to coma; but mild excitment, ataxia, and slurring speech may occur and lead to a suspicion of alcoholic intoxication. Chronic intoxication may produce vertigo, ataxia, diplopia, and a galaxy of physical signs, so that organic neurological syndromes are simulated, e. g. disseminated sclerosis or Parkinsonism. Mentally these patients often resemble chronic alcoholics. Phenobarbitone is specially liable to give severe and sometimes fatal skin eruptions. The eruption continues to spread when the drug is stopped. The standard treatment of acute barbiturate intoxication consists in stomach wash-outs and the administration of picrotoxin or a similar analeptic. Penicillin is given as a prophylactic against hypostatic pneumonia. Recently a form of treatment similar to that used in anesthetic overdosage—intubation or suction, oxygen therapy, and blood transfusion—has been advocated. It is said that the awakening effect of the analeptics is not sustained when doses well above anesthetic doses have been taken and that they lead to depression after initial stimulation.

Combined Corticotropin Therapy and Chemotherapy in Pulmonary Tuberculosis: With Special Reference to Hypersensitive Reactions. L. E. Houghton. Lancet **1**:595-598 (March 20) 1954.

Twenty-one patients with active pulmonary tuberculosis were given corticotropin in combination with streptomycin and *p*-aminosalicylic acid. Eight of them were known to have an acquired hypersensitivity to one or both of these drugs. The corticotropin suppressed all the reactions during a standard course of chemotherapy. On withdrawl of corticotropin, six of the eight patients had lost their hypersensitivity. Five of the 21 patients had gastrointestinal intolerance to *p*-aminosalicylic acid; this was suppressed by a very small maintenance dose of corticotropin. Five patients were given corticotropin in combination with streptomycin and *p*-aminosalicylic acid in the absence of hypersensitivity. Three patients in whom alarming hypersensitive reactions developed derived immediate benefit from corticotropin. No adverse clinical or radiographic effects were seen either during corticotropin therapy or after its withdrawal for periods of up to two years. During combined corticotropin therapy and chemotherapy, severely ill patients improved very much and the progress was maintained after withdrawal of corticotropin. Clinical and radiographic improvement was noted in patients who had not previously responded well to streptomycin and *p*-aminosalicylic acid alone.

Aluminum Hydroxide Granuloma After Immunization Against Tetanus. W. Beck. Medizinische **No. 11**:363-365 (March 13) 1954. (In German.)

Between April, 1952, and October, 1953, 37,000 active immunizations against tetanus were carried out among injured miners at the brotherhood hospital in Bochum, Germany. Of these, 27,000 were first injections with 0.5 cc. of aluminum hydroxide adsorbed tetanus toxoid (Tetanol) and 10,000 were second injections of 0.5 cc. of the same product given eight weeks after the first injection. The injections were made subcutaneously in the right breast. Of seven miners who reported the formation of nodules at the site of the injection, these nodules occurred 14 to 34 days after the first injection in five, and 2 and 14 days, respectively, after the second injection in two. Partly because of the fear of malignant tumors, the nodules in the skin of the breast were removed and examined microscopically, bacteriologically, and chemically. They were small and elastic and were located in the subcutaneous fatty tissue. They consisted of a relatively coarse cover from which septums were going toward the center, thus forming cavities that were filled with a yellowish, creamy, sterile substance. The cavities were lined with an epitheloid cell layer but in the lumen of the cavities there were observed single epitheloid cell nodules with some giant cells that contained foreign bodies of a homogenous appearance, turning bluish-purple on staining with hematoxylin. After staining with the weak alkali, alcoholic morin (2',3,4',5,7-pentahydroxyflavone), these structures showed a light green fluorescence on examination with the fluorescence microscope, a definite sign that they were aluminum compounds. The assumption that their formation might have been casual, being the result of a change in the constitution of the vaccine or because the vaccine was outdated, could be refuted by the facts that formation of nodules occurred with the use of vaccines of various dates, and that occasionally formation of structures similar to those observed in the tissues was observed in the tetanol vaccine. The author believes that the occurrence of these nodules in the seven miners was a manifestation of

hypersensitivity to the aluminum hydroxide, which would explain its very low incidence. The formation of the nodules should not be considered as a deficiency of the vaccine, in any case not with respect to the produced immunity, but it may be the morphological expression of a particularly strong antitoxin formation.

PATHOLOGY

Cortisone, Methylandrostenediol, and the Liver. L. Demeulenaere and R. J. Wieme. Acta gastro-enterol. belg. **17:**16-26 (Jan.) 1954. (In French.)

The effect on the liver of the simultaneous administration of cortisone and methylandrostenediol (17α-methyl-5: androstene-3β, 17β-diol) was studied as part of an investigation into the antagonism that may exist between cortisone and other steroids. Male mongrel rabbits weighing approximately 2 kg. at the start of the experiments were divided into three lots: animals in lot 1, which served as a control group, were given methylandrostenediol alone in doses of 5 or 10 mg. daily for periods of from 5 to 168 days; those in lot 2 were given moderate doses of both cortisone and methylandrostenediol (5 or 10 mg. of each daily) for from 33 to 179 days; and those in lot 3 were given a non-hepatotoxic dose of cortisone (5 mg. twice a week) and 5 mg. of methylandrostenediol daily for from 11 to 187 days. Comparison of the results obtained with those of earlier experiments in which cortisone was given alone showed that methylandrostenediol given in suitable doses reduces the necrotizing effect of cortisone on the liver parenchyma. Collagen development was demonstrated by Mallory's stain technique in cases in which reticulosis was present. Protein levels in the blood remained normal or were only slightly lowered, but certain profound disturbances in protein metabolism were revealed by the electrophoretic tracings. Especially noteworthy was the appearance of the supplementary fraction α^3, which is the most characteristic sign of the effect of cortisone on the lipoproteins. Lowering of the albumin fraction, however, was prevented, and the gamma fraction, though sometimes reduced, never disappeared. The antagonism, if any, that exists between the action of cortisone and that of methylandrostenediol can obviously not be expressed as a simple equation in which the mere administration of methylandrostenediol nullifies the catabolic effects of cortisone on the proteins. The frequency with which jaundice has been seen in patients treated with methylandrostenediol may perhaps be explained by the fact that bile excretion in animals receiving this substance was blocked by the presence of biliary thrombi. Similar intracanalicular thrombi were never found when cortisone alone was given.

Experimental Aspiration Pnumonia: III. Pneumonia Produced by Intratracheal Injection of Carbohydrate Solutions. R. H. Smith and T. J. Moran. A. M. A. Arch. Path. **57:**194-200 (March) 1954.

During experiments on the production of acute pulmonary edema in rabbits by intratracheal injection of milk, feeding mixtures, and sugar solutions, it was noted that in animals surviving the initial injection of the material pneumonia subsequently developed. The pneumonia produced by injection of sugar solutions was similar in many respects to that produced by injection of milk or solid foods. The present report describes this pneumonia. Intratracheal injections of varying concentrations of five carbohydrates (dextrose, lactose, maltose, dextrin, and fructose) and of several prepared feeding mixtures were given with sterile precautions to 36 healthy adult rabbits. Milk was not included in the feeding mixtures. The solutions, varying in strength from 6.25 to 50%, were injected into the trachea after the animals were anesthetized with ether. Twelve of the animals died of acute pulmonary edema and were excluded from this study. The animals that did not die of pneumonia were killed at varying times after aspiration by intravenous air injection. Seven control animals were given intratracheal injections of 5 cc. of sterile distilled water, and three animals were given intratracheal injections of 5 cc. of sterile 0.9% sodium chloride solution. Studies were made on the lungs of the experimental animals and of the controls. The reactions to the injected sugar solutions included acute pneumonia with abscess formation and empyema and mononuclear pneumonia with chronic granulomatous reaction, fibrosis, collapse, and emphysema. The pneumonia is similar to, but usually not so severe as, that produced by injection of similar amounts of milk. The authors feel that the practice of many pediatricians of substituting carbohydrate solutions for milk in the care of newborn infants with feeding problems would seem hazardous in view of the previously reported production of acute pulmonary edema in rabbits by intratracheal injection of strong carbohydrate solutions and the findings reported here of aspiration pneumonia caused by dilute sugar solutions.

RADIOLOGY

Manometer Assessment of Mitral Valve Disease. J. A. Aylwin. J. Fac. Radiologists **5:**178-181 (Jan.) 1954.

Pressure readings from the left auricle could be obtained until 1952 only at operation with the chest open. Allison evolved a technique for bronchoscopic puncture of the left auricle under local anesthesia, making it possible to obtain true records of pressures in this chamber. This can be repeated any number of times under relatively natural conditions. Control records have been obtained from patients about to be operated on for other disease; these show that, relative to the manubrium sterni, normal pressures are usually between +10 and -5 cm. H_2O. In mitral stenosis the range of pressures found has been from 23/17 to 75/50 cm. H_2O, while in mitral regurgitation figures as high as 85 cm. H_2O have been recorded during ventricular systole. Aylwin outlines the aid to investigation of mitral disease that may be obtained from probing the chambers of the heart with catheter and needle. These investigations are not always essential, for in straight-forward mitral stenosis surgery can be advised without elaborate pressure records. In cases of complex heart lesions or doubtful clinical signs additional information may be valuable. When mitral stenosis is associated with rheumatic damage to the aortic valve, it is important to decide how much disability can be attributed to each. High pressures in the left auricle would favor splitting the mitral commissures if the aortic lesion is not obviously gross. When mitral stenosis and regurgitation are combined, the problem of deciding which of the two is predominant has not yet been solved satisfactorily. The author feels that study of left auricular tracings will be more likely to supply the answer than any other investigation so far suggested, because gross regurgitation can be recognized as a large wave during ventricular systole. A considerable advantage to this investigation is that no recognizable complications have arisen from bronchoscopic puncture of the left auricle. On a few occasions, a large and tense pulmonary artery has also been punctured, but without subsequent trouble. Cardiac catheterization also supplies useful information in rheumatic valvular heart disease, but it also involves risks in patients ill with mitral disease. By combining clinical and radiological assessment with pressure records obtained from left auricular puncture and cardiac catheterization, we now have the means of diagnosing significant mitral stenosis with a high degree of accuracy, including the group of difficult cases that tax clinical judgment.

Roentgenologic Differential Diagnosis Between Chronic Mastitis and Mammary Carcinoma. C. M. Gros and R. Sigrist. Fortschr. Geb. Röntgenstrahlen **80:**50-65 (Jan.) 1954. (In German.)

Gros and Sigrist made roentgenograms on the breasts of 1,000 patients. They feel that roentgenologic examination should not be omitted when cancer of the breast is suspected. This is becoming more important, as women now generally present themselves earlier for examination of breast lesions. The small round nodule embedded in the glandular tissue so frequently seen today does not permit a diagnosis without exploratory excision. Roentgen study, however, generally clarifies the diagnosis without resort to biopsy, and, if the latter becomes necessary for corroboration, roentgen study permits localization

of the suspected site. Psychological factors are also involved in the earlier diagnosis of breast carcinoma by roentgen study, because women more readily agree to roentgen examination than they do to exploratory excision. The authors give particular attention to the roentgenologic differentiation between chronic mastitis and carcinoma. They describe the technique of roentgen examination and the roentgenologic appearance of normal breasts, of those with chronic mastitis and with mammary carcinomas on the basis of 16 case histories. Cysts in chronic mastitis, mostly multiple and bilateral, produce a sharply outlined homogeneous density. The scirrhous type of carcinoma shows a shadow with an irregular outline and with spicules extending into the soft tissue. In the encephaloid type of mammary cancer an irregular, nonhomogeneous shadow is seen. Small calcifications scattered throughout the tissue represent calcified necroses of foci of carcinoma cells.

Creeping Eruption Associated with Transient Pulmonary Infiltrations. E. H. Kalmon. Radiology **62:**222-226 (Feb.) 1954.

Creeping eruption, known also as endemic cutaneous helminthiasis and larva migrans, is endemic in the coastal areas of the southeastern United States. It is characterized by tortuous, elevated, migrating burrows or tunnels in the skin with intense itching. Moderate cellulitis due to secondary infection is common. The case cited suggests that it may be the causative agent of Loeffler's syndrome. The patient, a man aged 23, noticed multiple papular lesions on his legs, arms, and back, which became erythematous and pruritic the following day. Typical migrating burrows of creeping eruption soon appeared. All lesions grew worse, and many became secondarily infected. An annoying nonproductive cough developed, occurring in paroxysms, and there was an associated mild dyspnea. The patient was hospitalized. In addition to the skin lesions, he now had bilateral wheezing and crepitant rales. The following day all skin lesions were sprayed with ethyl chloride, after the man had received thiopental (Pentothal) sodium anesthesia. There was a low-grade fever for seven days. The moderately severe cough continued for approximately two weeks. The first roentgen examination of the chest showed widely scattered patches of bronchopneumonia in each lung. Three days later the left lung had almost cleared, as had the right upper lung field, but the right base showed more extensive infiltration. The white blood cell count was 13,750, with 66% neutrophils and 3% eosinophils. Six days later the corresponding values were 17,400, 74%, and 11%. Ancylostoma ova were found twice in the patient's stools, suggesting that the larval forms can traverse the lungs to produce the fleeting pulmonary infiltrations associated with Loeffler's syndrome. The patient was discharged on the 18th day. The cause of Loeffler's syndrome has not been firmly established, but it is probably an allergic response by the lungs to various antigenic substances. Causative agents that have been suggested are privet pollens, Endameba histolytica, Ascaris lumbricoides, Trichuris trichiura, Strongyloides, Taenia saginata, brucellosis, azosulfamide, Necator americanus, and creeping eruption.

Irradiation of Eczema Through Perforated Screen. K. Bezold. Strahlentherapie **93:**434-439 (No. 3) 1954. (In German.)

Bezold mentions an incident that suggested the possibility that irradiation therapy of eczemas and dermatoses could be carried out while the skin was to a great extent protected against rays. Irradiation was given through lead screens that had circular perforations from 2.5 to 3 mm. in diameter. In the screens used at first, the apertures accounted for 28% of the surface and in those used later for 20%. A rubber plate applied to the skin side of the perforated lead screen filtered out excessively soft secondary irradiation. The irradiation was usually performed with 50 kv., produced in a tube with a beryllium window. Individual doses were usually 100 r, sometimes 150 r, and were given up to three times at intervals of 8 days. In some patients with eczematous lesions on both hands, the right hand was irradiated with the perforated screen, the left hand without it. Roentgen irradiation through the perforated screen was given to 111 patients with eczema. It was found that the therapeutic effect was equivalent to that obtained with "full" irradiation. Futhermore, the method seemed helpful in other skin lesions such as acne and dyshydrosis. Tolerance for irradiation was good in all patients treated by the screen method, and no exacerbations resulted from the irradiation. The percentage of patients who were refractory to irradiation was about the same with or without the screen.

The Saskatchewan 1,000-Curie Cobalt ^{60} Unit. T. A. Watson, H. E. Johns and C. C. Burkell. Radiology **62:**165-176 (Feb.) 1954.

Watson and co-workers state that the 1,000 curie cobalt 60 unit in use at the Saskatoon Cancer Clinic, Saskatchewan, Canada, consists of a spherical lead-filled steel casing 22 in. in diameter. Inside the casing is a wheel of heavy metal and lead, having at one point on its perimeter a cobalt source 1 in. in diameter and ½ in. thick. A tapered opening leads from the perimeter of the wheel through the lead to the exterior. When the cobalt is opposite this opening, a collimated beam escapes; when the wheel is rotated 180 degrees, the cobalt is shielded by 7 in. of "heavy metal," and the machine can then be considered as "turned off." To turn it on, an electric clock is set to the desired exposure and a switch is turned. The wheel then rotates to the "on" position, and when it reaches this point the clock starts. When the required treatment time has elapsed, the wheel rotates back to the "off" position. By means of suitable treatment cones, various fields of 5 by 5 to 15 by 15 cm. can be obtained at 80 cm. source-skin distance. Larger fields can be obtained by increasing the source-skin distance. The final limiting diaphragm is located 15 cm. from the skin, so that the surface dose from secondary electrons is virtually eliminated. The output is approximately 30 r per minute at this distance. Since cobalt 60 has a half-life of 5.3 years, the output falls 1.1% per month. Calibration charts are prepared for each month. Comparisons were made between the physical properties of cobalt 60 radiation and that produced at 200 kv., 3 mev, and 25 mev. Cobalt 60 radiation and 3 mev x-rays are similar from the point of view of therapeutic application, however, when one considers integral dose, surface dose, depth dose, differential absorption of bone and cartilage, the advantages of a high-energy source, such as cobalt 60, are obvious. The increased skin tolerance is probably due to the fact that the maximum dose does not fall on the surface of the skin, but occurs 4 to 5 mm. below the surface. The authors are using the cobalt unit on a routine rather than an experimental basis and believe that it is indicated particularly for deep-seated tumors, where the higher depth dose can be used to advantage, and in tumors that are adjacent to bone or cartilage, since the differential absorption of these structures, compared with soft tissues, is almost at a minimum at this energy level.

Skin Effects of Cobalt 60 Telecurie Therapy. C. C. Burkell, T. A. Watson, H. E. Johns and R. J. Horsley. Brit. J. Radiol. **27:**171-176 (March) 1954.

The 1,000 curie cobalt 60 unit was used by Burkell and co-workers to supplement the gamma radiation of radium to the parametrium in carcinoma of the cervix, in treating carcinoma of the larynx, bronchus, urinary bladder, esophagus, and other deep-seated tumors, as well as in the postoperative treatment of carcinoma of the breast. Fields of various sizes were used, and beam directional techniques were employed wherever possible. Treatments were given with and without plaster jackets and wax and with and without "bolus" material. They were given with and without "covers" to the applicator ends. Patients were treated over a three week period, receiving equal daily doses divided into 15 exposures. The output of the unit was approximately 30 r per minute at a source-to-skin distance of 80 cm. and a half-value layer of 1.1 cm. of lead. The skin reactions in general have been less pronounced than what would have been expected had 200 or 400 kv. radiation been used. This was true even when fewer fields were employed and, in many cases, a higher tumor dose achieved. For instance, in the postoperative treatment of the axilla and supraclavicular fossa of patients

with carcinoma of the breast, a central tumor dose of 4,000 r in three weeks was easily attained with a much less pronounced skin reaction than when a 3,750 r tumor dose was achieved with 400 kv. radiation. In most cases with Co^{60} radiation, there was only erythema followed by a dry desquamation. A few of the fatter patients showed patchy areas of moist epitheliitis. In patients with carcinoma of the larynx, the milder skin reaction was particularly noticeable on the posterolateral fields. A number of patients with extensive carcinoma superficially placed, such as carcinoma of a parotid gland with cervical metastases, were treated. Even though a dose as high as 5,000 r was applied to a single field (15 by 10 cm.) over a three week period, the skin reaction was nothing more serious than a pronounced erythema followed by a dry desquamation. Clinical experiments were carried out with open-end and closed-end applicators using the Co^{60} telecurie unit. These experiments indicate that the radiation delivered to the surface of the skin is very important in producing a skin reaction. Consequently, to minimize skin reactions from supervoltage sources, the "build-up" ratio in the first few millimeters of tissue should not be destroyed by having closed ends on the applicators.

ANESTHESIA

Electrocardiographic Changes During General Anesthesia. C. Fisch, M. E. Pickett and R. B. Failey Jr. J. Indiana M. A. **47**:121-126 (Feb.) 1954.

Electrocardiographic studies are reported on 26 patients undergoing a variety of surgical operations, but not open thoracotomy or operations involving head and neck. The ages ranged up to 84 years. Equipment consisted of a Cambridge operating room cardioscope. This apparatus includes a direct-writing electrocardiograph. A cathode ray oscillograph permits continuous visualization of the electrocardiograph tracing on a glass screen. Control tracings were taken for all patients prior to induction of anesthesia. From this point the electrocardiogram was observed continuously on the glass screen, and tracings were recorded instantaneously whenever any abnormality or significant change was observed. The anesthetic was invariably an inhalant, gas-oxygen-ether in most cases and cyclopropane-ether in two. Morphine and atropine in standard dosage were given preoperatively. Some electrocardiographic abnormality developed in 18 patients while they were anesthetized. This incidence is about the same as that observed by other investigators. Conditions unlike those typically associated with primary myocardial disease appear to be responsible for electrocardiographic change under anesthesia and for sudden cardiac deaths during anesthesia. These alterations seem to depend not primarily on the heart itself but on abnormal activity of certain extracardiac reflexes that influence cardiac rate and rhythm. In man and in various animals there exist a wide variety of these reflexes whereby stimulus of a peripheral nerve ending results in the discharge of central autonomic nervous impulses so as to influence heart rate or rhythm. The electrocardiogram may show various types of block such as prolonged PR interval and disappearance of P waves. Occasionally conduction is also blocked at the auriculoventricular node, the electrocardiographic result being either a transient complete heart block or a compensatory idioventricular rhythm. The clinical result is frequently that of syncope, occasionally convulsions, and, if uncorrected, sudden cardiac death. Prophylaxis rather than treatment is the logical approach. Good preoperative sedation, adequate oxygen, and, during induction, the avoidance of manipulations that may trigger reflexes are all important. Intravenous administration of procaine and its derivatives, procaine amide (Pronestyl) hydrochloride and diethylaminethanol, reduces the incidence of cardiac arrhythmias by inhibiting vagal effects and have proved useful. Digitalis and quinidine are of very limited value in anesthetic emergencies. Chloroform and ethyl chloride should be used with care, particularly when epinephrine or other sympathomimetic drugs may be needed. The combination of procaine locally and a general anesthetic or of curare and a general anesthetic have the effect of making possible surgical manipulations at levels before deep anesthesia is reached. Reflex activity is at its height during light anesthesia, and under such circumstances the danger of cardiac arrest is great.

PHYSIOLOGY

The Work of Breathing in Normal Subjects. M. B. McIlroy, R. Marshall and R. V. Christie. Clin. Sc. **13**:127-136 (Feb.), 1954.

According to McIlroy and associates, the methods of measuring the work of respiration can be divided into three main groups. First, the increased oxygen consumption resulting from hyperventilation can be measured, but this is subject to many inaccuracies. Second, the intrapleural or intraesophageal pressure and the tidal volume or rate of air flow may be recorded and by plotting volume change against pressure change the work of breathing can be measured directly. With this method the work done on the lungs only is measured, and no account is taken of the work involved in moving the chest wall and adjacent viscera. Third, passive respiration may be produced in a Drinker type of respirator and measurements made of the pressure in the respirator and the volume changes of the lungs. This method measures the total work of respiration, but its main disadvantage is that it can only be applied to passive respiration. The work described is confined to measurement of the work done on the lungs only. The work required to ventilate the lungs was measured from simultaneous records of intraesophageal pressure and tidal volume in normal subjects at rest and on exercise. The work of breathing at rest is about 0.3 kilogram meter per minute and the maximum work is about 80 kilogram meters per minute. This last figure, which the authors obtained by direct measurement of the work done on the lungs during maximum voluntary ventilation, indicates that the maximum rate of work of which the respiratory muscles are capable is about 270 times greater than the rate of work in the resting state. On exercise, the work of ventilating the lungs increases linearly with the increase of minute volume. The rigidity of the lungs and the resistance to air flow decrease on exercise. The existence of an optimal rate of respiration at which a given alveolar ventilation is maintained with a minimal expenditure of work has been shown directly both at rest and on exercise. Normal subjects at rest and on exercise breathe at the rate and depth that is most economical in in terms of respiratory work. The regulating mechanism that brings about this control is not yet elucidated.

The Work of Breathing in Mitral Stenosis. R. Marshall, M. B McIlroy and R. V. Christie. Clin. Sc. **13**:137-146 (Feb.) 1954.

The work required to ventilate the lungs was measured from simultaneous records of intraesophageal pressure and tidal volume in patients with mitral stenosis at rest, on exercise, and on lying flat. In patients with cardiac failure, dyspnea and orthopnea are associated with a substantial increase in the amount of work required to ventilate the lungs because they become more rigid. In cardiac failure the patient breathes at the rate and depth that is most economical in terms of respiratory work. This is true of the rapid and shallow breathing of exertional dyspnea as well as the change in respiratory rhythm that occurs in orthopnea.

The Work of Breathing in Emphysema. M. B. McIlroy and R. V. Christie. Clin. Sc. **13**:147-154 (Feb.) 1954.

The work required to ventilate the lungs was measured from simultaneous records of the intraesophageal pressure and tidal volume at rest and on exercise in patients with emphysema. The results were compared with those in young normal subjects and in those over the age of 50. In emphysema there is a relative increase in the nonelastic resistance of the lungs to ventilation, and as a result the respiratory work on hyperventilation is greatly increased. This abnormal increase in respiratory work must at least be an important factor in the production of dyspnea and in the limitation of the maximal breathing capacity. Experiments with hydrogen indicate that the increase in nonelastic resistance is not wholly due to bronchial obstruction; it is due in part to a change in the viscoelastic properties of the lung that is presumably irreversible.

BOOK REVIEWS

Surgical Infections: Prophylaxis—Treatment—Antibiotic Therapy. By Edwin J. Pulaski, M.D., D.M.Sc. (Surgery), Lieutenant Colonel, Medical Corps, United States Army. Publication number 170, American Lecture Series, monograph in Bannerstone Division of American Lectures in Surgery. Edited by Michael E. De Bakey, M.D., Professor of Surgery and Chairman of Department of Surgery, Baylor University College of Medicine, Houston, Texas, and R. Glen Spurling, M.D., Clinical Professor of Surgery, University of Louisville, Louisville, Kentucky. Cloth. $7.75. Pp. 332, with 10 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, 1954.

In the foreword to this important volume, Dr. Michael E. De Bakey has stated: "The recent development and present availability of a number of effective antimicrobial agents have produced a tendency to shift the emphasis in surgical infections to these agents and away from the sound surgical principles by which little more than a decade ago all of them were exclusively managed. This is a tendency which must be recognized and controlled without loss of time. . . . There can be no doubt that in the management of surgical infections these new agents achieve their greatest effectiveness when they are used as they should be, that is, in combination with surgical measures of established worth." This monograph was originally planned as a small manual on antibiotic therapy, but it has become a larger volume dealing with many aspects of surgical infections. The major emphasis is on surgical principles and practices. The author has accepted the fact that antibiotic therapy should be adjunct therapy and not a substitute for sound surgical measures. The volume consists of eight chapters, which are divided into two parts. There is an excellent bibliography at the end of each chapter. An appendix provides a reference for the tables and a list of general references. There is an excellent index. The entire field of surgical infections is covered in an adequate manner. The volume is both a handbook on the background of surgical infections and a practical presentation of the control and treatment of the major infections of a surgical nature. Emphasis is constantly placed on the fact that antibiotic therapy is useful chiefly when it is used in conjunction with sound surgical principles. This small volume provides a mass of material that every surgeon must have available if he is to practice surgery intelligently.

Experimental Surgery Including Surgical Physiology. By J. Markowitz, M.B.E., M.B., Ph.D., Associate Professor of Physiology, University of Toronto, Toronto, Canada. In collaboration with J. Archibald, D.V.M., M.V.Sc., Professor and Head of Division of Small Animal Medicine and Surgery, Ontario Veterinary College, Guelph, and H. G. Downie, D.V.M., M.S., M.V.Sc., Assistant Professor of Physiology, Ontario Veterinary College. Third edition. Cloth. $10. Pp. 851, with 554 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1954.

This new edition presents physiological problems in the surgery of animals and man, and in it the emphasis has been shifted from mammalian physiology toward human physiology. It has become a useful reference book in the teaching of surgery, as it includes many techniques devised on animals that subsequently have been applied to man. It is generously sprinkled with illustrations and is as current as is possible. Earlier editions emphasized the physiology of the gastrointestinal tract and the circulation and experimental observations relating to physiological disturbances of these systems in man. In addition to these subjects, physiological material and surgical progress relating to the respiratory system, the heart, the great vessels, and the kidney have been added or expanded. At a time when emphasis on physiological research and teaching is shifting from total body and organ physiology to the cellular level, this book should be especially welcomed by the surgeon, who must continue to think of the entire patient and his organic disease. An analysis of the material presented in the three editions reflects the fact that in the last decade many of the advances in organic physiology have been made by surgeons. If this trend continues, the physiologist in the future will become dependent on the surgeon for his information in general physiology. The book is well written and is broad in coverage. Most of the plates are excellent, and other documentary information is more than adequate. The style of writing is effective, but is a curious combination of pragmatic science enlivened by a number of classical quotations and mottos. This book can be recommended without reservation to the surgeon and the investigator. It will serve as a useful reference book to the physician and student, particularly on problems dealing with cardiovascular surgery and gastrointestinal physiology.

Electrocardiographie clinique. Par J. Lenègre, professeur à la Faculté de médecine de Paris, G. Carouso, chef du laboratoire d'electrocardiographie, et H. Chevalier, ancien chef de clinique à la Faculté de médecine de Paris. Préface du Pr Ch. Laubry. Cloth. 7600 francs. Pp. 810, with 341 illustrations. Masson & Cie, 120 boulevard Saint-Germain, Paris, 6e, 1954.

This monograph is devoted to practical electrocardiography and its role in clinical diagnosis. Fundamentals of electrophysiology of the heart and theoretical concepts pertinent to the interpretation of the electrocardiogram are dealt with in two initial sections that include a general discussion of vectorcardiography. According to the authors, this method is merely a research tool that cannot replace conventional electrocardiography in practice. The subject is presented in an original and didactically excellent way. The book is divided into three main sections: the first dealing with electrocardiographic syndromes, the second with heart diseases classified as to cause, and the third with cardiac arrhythmias. Each section contains a concise text with cross references to representative electrocardiograms assembled at the end of its subdivisions. The tracings are explained in extensive legends that also give clinical data, autopsy findings, and a final critical evaluation of the importance of the electrocardiogram in each case.

Unfortunately, the book loses part of its teaching value owing to preferential selection of the material, which reflects largely the personal interests of the authors and of the French school in general in the past decade. Thus, the electrocardiographic manifestations of cardiac hypertrophy, rheumatic heart disease, hypertension, cor pulmonale, coronary disease, and myocardial infarction are covered exhaustively, but the reader will miss an adequate discussion of drug effects, the electrocardiogram in electrolyte imbalance, and the less specific abnormalities that represent a good deal of electrocardiographic practice. Surprisingly enough, and contrary to old French tradition, the section on cardiac arrhythmias is very weak and superficial, conspicuous only by misinterpretation of even simple arrhythmias (such as figures 306b and 337b, considered erroneously as complete A-V dissociation, or the "nodal escape" in figure 325). The bibliography is ample, although not always fortunate in the selection of references with regard to their importance. Despite these limitations, this superbly illustrated monograph gives a good account of most of the important aspects of clinical electrocardiography.

Adaptation in Micro-Organisms: Third Symposium of the Society for General Microbiology Held at the Royal Institution, London, April 1953. [E. F. Gale and R. Davies, editors.] Cloth. $6. Pp. 339, with illustrations. Cambridge University Press, Bentley House, 200 Euston Rd., London, N.W. 1; American branch, 32 E. 57th St., New York 22, 1953.

Arranged in 15 chapters, with discussion immediately following the text of each lecture, this volume gives adequate coverage to a specialized field that has been intensively developed in the past 10 years. From the different types of evidence advanced on mechanisms of adaptation it is clear that extreme views held only a few years ago by the so-called genetical school and the environmental school are being modified to meet in a more rational area. Mutational selection and environmental modification of phenotypic expression of growth form and metabolism are not mutually exclusive conditions, but often

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These book reviews have been prepared by competent authorities but do not represent the opinions of any official bodies unless specifically so stated.

complementary, as is well brought out in discussions by G. Pontecorvo, S. Spiegelman, and C. N. Hinshelwood. In a symposium on so restricted a topic some overlapping may be expected, but, on the whole, the organizers are to be complimented on their selections. The chapters by E. P. Abraham (The Development of Drug Resistance in Microorganisms); Mary Barber (Antibiotic-Resistant Staphylococcal Variants); and D. A. Mitchison (The Ecology of Tubercle Bacilli Resistant to Streptomycin and Isoniazid) are noteworthy. A group of papers by Cohn and Monod, Spiegelman and Halvorson, and M. R. Pollock deals with enzyme biosynthesis and genetic control thereof. This area of investigation is now changing from one in which fascinating hypotheses held sway to one in which factual information has become available from ingenious experimental approaches devised by these workers. The inclusion of chapters on adaptations in paramecia (G. H. Beale), in thermophilic microorganisms (L. F. L. Clegg and S. E. Jacobs), and in fungi (W. Brown and R. K. S. Wood) serves to broaden the approach of the symposium. These contributions, dealing with less highly cultivated areas, indicate the importance for adaptation of such mechanisms as heterocaryon formation in filamentous fungi and cytoplasmic reorganization in many protozoa. The volume, as a whole, maintains the high standard of excellence set by the two preceding symposiums of the Society for General Microbiology and may be expected to receive careful attention from a wide audience.

Congenital Heart Disease: An Illustrated Diagnostic Approach. By Henry S. Kaplan, M.D., Professor of Radiology, Stanford University School of Medicine, San Francisco, and Saul J. Robinson, M.D., Assistant Clinical Professor of Pediatrics, Stanford University School of Medicine. Cloth. $12.50. Pp. 126, with 146 illustrations; drawings by Zena Kavin. McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E.C.4, 1954.

The authors have undertaken the difficult task of presenting a highly technical subject in simple and nontechnical terms. The book is written as an introduction to congenital heart disease and is divided into two parts. In the first part a fairly good but brief approach to the subject is made. A few useful hints are given on how the physician should consider each case and what he should look for and avoid. Next are considered laboratory tests, roentgenology, the electrocardiogram, and special procedures such as angiocardiography and cardiac catheterization. A few words are devoted to the surgical treatment of certain malformations. The section on roentgenology is excellent and is the best aspect of the whole book. The paper, format, choice of illustrations, and reproductions are also excellent. Emphasis is placed on pediatric roentgenology. The part on electrocardiography is inadequate. The dangers of angiocardiography and cardiac catheterization are overemphasized. The statement that "the withdrawal of 15 or more 10 cc. blood samples, particularly in the child, may result in anemia, which may have to be corrected by blood transfusions" is absurd. Actually, blood oxygen determinations require only 2 to 3 cc. of blood at most, and it is not always necessary to withdraw 15 samples. No mention is made of the newer techniques in cardiac catheterization, such as the use of the photoelectric oximeter and dye dilution curves.

In the second part the authors limit the presentation to typical forms of the most common malformations, with a brief enumeration of the salient features and a representative electrocardiogram. The use of drawings to enable the reader to interpret the roentgenograms will be greatly appreciated. The reader should bear in mind that the more atypical or complicated cases have been deliberately avoided. The bibliography is scant and refers only to books and papers of general interest. Other criticisms of a minor nature may be made. The authors' description of the circulatory dynamics in each malformation is inadequate. In the chapter devoted to interventricular septal defect the impression may be gained that such malformations are usually benign. Actually, they are often dynamically significant and may even be disabling. The authors fail to differentiate between right ventricular hypertrophy and right bundle branch block, which may be of the utmost importance in the differential diagnosis. The authors fail to emphasize pulmonary hypertension, which is a frequent finding or complication of several malformations. Too much space is devoted to malformations of the aortic arch, which are relatively rare and clinically insignificant. This book should be of use to the general practitioner or pediatrician who would like to know a little more about congenital heart disease. It is not for the specialist.

Clinical Roentgenology. Volume I: Developmental and Systemic Conditions and Local Lesions in the Extremities. By Alfred A. de Lorimier, M.D., Radiologist, St. Francis Memorial Hospital, San Francisco, California, Henry G. Moehring, M.D., Radiologist, Duluth Clinic, Duluth, Minnesota, and John R. Hannan, M.D., Radiologist, Cleveland, Ohio. Cloth. $18.50. Pp. 492, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Illinois; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1954.

The authors have collected a large amount of material covering roentgenology of the extremities. This was drawn from their own services and from other services throughout the country; the Army Institute of Pathology, Walter Reed Army Hospital, and Cleveland Clinic Foundation Hospital are among the many excellent sources of material. The volume is divided into 11 major sections dealing with the extremities, developmental malformation, traumatic lesions, metabolic disorders, endocrinopathies, infections, neoplasms, blood dyscrasias, arthropathies, and special studies. The latter includes venography and sinus injection. Under these classifications almost the entire field of bone roentgenology is covered. The pattern of discussion includes general consideration, roentgenographic manifestation, clinical corroboration, laboratory corroboration, differential consideration, and references. The text is brief and pertinent under each subtitle, so that the reader can acquaint himself at a glance with all the phases of the diseases described. The outstanding feature of the volume is the profusion of excellent illustrations. Although this book should be of special value to roentgenologists because of the excellent illustrations and coverage, others interested in bone pathology should find it of great interest.

Electrical Methods of Blood-Pressure Recording. By Frank W. Noble, M.E.E. Publication number 155, American Lecture Series, monograph in American Lectures in Medical Physics. Edited by Otto Glasser, Ph.D. Cloth. $3. Pp. 56, with 12 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1953.

The simple methods ordinarily used to measure the mean arterial blood pressure and to record its fluctuations serve some purposes very well but involve systems too heavy and sluggish to satisfy the needs of modern research. By means of the electrical manometers and networks described in this book, it is possible not only to follow rapid oscillations with high fidelity but also to obtain the first and higher order derivatives of pressure with respect to time. The concepts of overshooting, natural frequencies, and critical damping are clearly presented in an opening chapter; subsequent chapters discuss transducers, amplifiers, recorders, and differentiating and integrating circuits. There is a summary, bibliography, and index. The book will be indispensable to physiologists working in hemodynamics.

Clinical Endocrinology. By Karl E. Paschkis, M.D., Associate Professor of Medicine, Jefferson Medical College, Philadelphia, Pennsylvania, Abraham E. Rakoff, M.D., Clinical Professor of Obstetrics and Gynecologic Endocrinology, Jefferson Medical College, and Abraham Cantarow, M.D., Professor of Biochemistry, Jefferson Medical College. Cloth. $16. Pp. 830, with 253 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 East 33rd St., New York 16, 1954.

While several other recently issued texts represent the efforts of a large group of contributors with a resultant variation in clarity of exposition and a distribution of space disproportionate to the importance of the problem, the authors of this book have succeeded in amalgamating their personalities to produce a smoothly flowing text that follows the traditional anatomic and physiological considerations of the major endocrine glands and their functional or dysfunctional interrelationship. The result is a fine combination of clinical experience with physiological and biochemical explanations of the phenomena encountered in diagnosis and treatment, told in understandable language. This excellent, well-illustrated teaching text should also be of value to the practicing physician.

QUERIES AND MINOR NOTES

ESTROGENS FOR PROSTATIC CANCER

To the Editor:—*A patient has been receiving estrogens for several years for prostatic carcinoma. His breasts have become large and sensitive. Since chlorotrianisene (TACE) therapy was begun four months ago, the sensitivity has gone from his breasts. Can the breast size be expected to diminish?*

Milton Vainder, M.D., Chicago.

Answer.—Gynecomastia, or enlarged painful breasts, is not uncommon in patients who are treated for any length of time for carcinoma of the prostate with estrogen administration. It has been our experience that there is less pain in the breasts and somewhat less swelling with chlorotrianisene than some of the other estrogen preparations. The size of the breasts will probably not diminish to any great extent as long as the patient is receiving estrogen therapy, even though the sensitive reaction may have disappeared. There is an individual variation to reactions to estrogen therapy. The enlargement of the breasts and the sensitive reaction to prolonged estrogen therapy are the only known indications that the patient is actually neutralizing the androgen.

ESTIMATE OF PENICILLIN REQUIREMENTS

To the Editor:—*In my position I am involved with procurement of medical supplies for 11,000 persons. I have estimated our penicillin requirement as about 100 million units per month. Some opinion exists that this is excessive, but I believe it is a minimum. Acute infections due to streptococci and pneumococci are common. Can you tell me how much penicillin per month or per year is used in the average American city of 11,000? Any other comments on the problem of penicillin use in this era of close scrutiny of government expenditures will be welcome.*

D. Kirkham, M.D., Majuro, Marshall Islands

Answer.—Your estimated penicillin requirements of 100 million units per month for 11,000 persons is not excessive. Actually the estimate is entirely too low and would not meet even minimum requirements. One case of subacute bacterial endocarditis would sadly deplete your supply of 100 million units monthly. In reliable figures based on the requirements of 1,000 men per month and arrived at after several years of experience, the requirement per month is a total of 187,830,000 units and for 11,000 persons would be 2,066,130,000 units.

CASTRATION AND CANCER OF THE BREAST

To the Editor:—*What are the current opinions on the advisability of castration in cases of carcinoma of the breast?*

John L. Atlee Jr., M.D., Lancaster, Pa.

Answer.—Surgical castration in premenopausal women with metastatic breast cancer induces remissions in about 50% of cases. The average duration of the remissions is about nine months. Patients who benefit from castration will frequently obtain further successive remissions from adrenalectomy, androgen therapy, and cortisone therapy. Premenopausal women who fail to benefit from castration are also not helped by adrenalectomy. Cortisone therapy will induce significant temporary remissions in some of these patients. Estrogen therapy is occasionally helpful, but androgen therapy is rarely of benefit. In postmenopausal women with metastatic breast cancer, castration should be combined with adrenalectomy. Remissions are obtained in 40% of the patients with the combined procedure. Patients who benefit from castration and adrenalectomy may obtain subsequent remissions from androgen and cortisone therapy. Postmenopausal women who fail to benefit from castration and adrenalectomy will frequently obtain remissions from estrogen therapy.

The available data suggest that prophylactic castration may delay the appearance of metastatic lesions in some patients. There is no evidence that surgical castration induces harmful effects on the growth of the cancer. Surgical castration is preferred over x-ray castration, since radiation is an uncertain means of completely eliminating ovarian function.

POSITIVE SEROLOGIC TEST FOLLOWING VIRUS PNEUMONIA

To the Editor:—*A 23-year-old man without any history of syphilis had virus pneumonia in October, 1953. A premarital Kahn reaction in the following December was 4+. Two different laboratories made several tests (Wassermann, Kahn, and Mazzini). All reactions were 4+. I would appreciate your opinion.* *Jules Boruchowitz, M.D., New York.*

Answer.—Virus pneumonia may lead to a false positive serologic reaction. Generally, the reaction becomes negative in the course of several months. It is likely that, if the young man were reexamined now, the reaction would be negative; if weakly positive, the reaction should reach negativity a few weeks hence. If the reaction at this time is still 4+, the possibility of syphilis has to be considered. If a quantitative serologic test had been made in the initial examination, and the quantitative titer on repeated examinations at different intervals were found to be dropping, that would be an indication that the serologic reaction was the result of the virus pneumonia. It is assumed that no quantitative serologic test had been made on the blood specimen of this young man. In that case, a Treponema pallidum immobilization test would help in the differentiation of a true and false positive reaction.

SWELLING OF LEG

To the Editor:—*A 16-year-old girl complains of unilateral swelling in her calf and thigh with exertion. Her leg is not painful except when swollen. There are no superficial varicosities, and results of a pelvic examination, blood cell count, sedimentation rate, chest roentgenogram, urinalysis, and serologic studies are all within normal limits. My diagnosis is a deep venous insufficiency, and she is now wearing an elastic stocking. Would surgery of any type be indicated in this case?*

M.D., California.

Answer.—Unilateral edema of the lower extremity may be due to deep venous insufficiency or to lymphatic obstruction. It would be rather unusual for a deep venous insufficiency to be associated with no superficial varicosities, especially after exercise, and possibly the dorsal veins of the foot do show distention after rapid exercise such as standing on the toes 10 to 15 times. Such venous insufficiency is usually congenital in origin owing to the absence or weakness of iliofemoral valves, and only phlebography can really demonstrate it. A history of injury or deep iliofemoral thrombosis would, of course, be highly pertinent. Lymphedema may be due to congenital absence of valves, to low-grade obstructive lymphangiitis following fungus infections of the toes or vagina, or to glandular hyperplasia in the groin or pelvis. If lymph nodes are palpable in the groin, a biopsy is advisable, since Hodgkin's disease, leukemia, or lymphosarcoma may first manifest themselves by lymphedema. The cosmetic effect of treatment is never too satisfactory. A well-fitting elastic stocking has to be worn from toes to groin all day, with elevation of the foot of the bed at night, salt restriction, and weight reduction. Anemia, hypoproteinemia, and a low metabolic rate need attention. Surgical treatment should be deferred until a more positive diagnosis is made.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

PULMONARY FIBROSIS AND EMPHYSEMA

To the Editor:—*For 12 years I have had dyspnea on going uphill. I gave up smoking and my condition slightly improved, but in 1947 a roentgenogram of my lungs showed emphysema. In 1950 I had pneumonia of the right lung, and since then I have had asthmatic attacks. On my doctors' advice, I went to Mont Dore in France for spring-water cure but without improvement. I went to Paris and stayed at the Broussais Hospital for 40 days. The roentgenogram showed emphysema and fibrosis of the lungs. The diagnosis was "Asthma d'effort." In the above-mentioned hospital I was treated with corticotropin (ACTH), but did not improve. My French doctors advised me to continue with corticotropin after my return to Cyprus, which I did for 10 months, but the relief lasted for only an hour every day. In February, 1953, I went to the American University Hospital in Beirut, but they could not relieve me. I have stopped corticotropin therapy (although my French doctors have written me to continue it indefinitely) and I take ephedrine for relief, although those doctors are against it. I have to take sleeping pills, for just a few hours of sleep. Also when 20 years old, I had pleurisy, which caused adhesions on the right side of thorax. At present I cannot take even a few steps. I hope this short history will enable you to give advice as to what can be done to relieve my continued suffering.*

Eugenios Papadopoulos, M.D., Nicosia, Cyprus.

Answer.—In conditions of pulmonary fibrosis and emphysema, the use of corticotropin (ACTH) need be continued only if subjective improvement or objective measurement of pulmonary function is altered favorably. Liberal use of drugs that relieve symptoms and findings of bronchospasm should be encouraged. If respiratory tract infections are frequent, residence in a warm dry climate may be beneficial. If purulent sputum is a constant finding, the cultivation of predominant organisms and testing of their sensitivity to the various antibiotics may point the way to control of the element of infection when present. Breathing exercises, especially those that develop muscles of the abdominal wall, may assist in elevation of the diaphragms and improve their efficiency. When oxygen therapy is necessary, it is best administered by means of a positive pressure device such as the Bennett valve to improve ventilation and assist in the disposal of excess carbon dioxide accumulation while improving arterial oxygen saturation. The more advanced stages of pulmonary emphysema are irreversible but prolongation of life and comfort frequently is possible.

DIFFERENTIAL COUNTS

To the Editor:—*Twenty-five years ago I was taught that the normal polymorphonuclear percentage was 60 to 70 and the normal lymphocyte percentage was 20 to 30. Recent textbooks repeat these figures. In the last 20 years I have noted that the polymorphonuclear percentage is reported consistently less and the lymphocyte percentage consistently more than the above figures. At first I assumed that this meant that the patient's "resistance" was lowered. After a time I assumed the books were wrong, and, finding no confirmation of such a concept clinically made no effort to raise the polymorphonuclear percentage. Now our medical director repeats this concept that a low polymorphonuclear count indicates lowered resistance. I would appreciate your opinion on normal differential counts and on the lowered resistance concept.*

M.D., New York.

Answer.—One cannot base a diagnosis on mild deviations from the stated normal values for differential counts, in the absence of supporting findings. Furthermore, Osgood and coworkers (*Arch. Int. Med.* **64**:105, 1939) found that the average percentage of polymorphonuclears in healthy young adults was 54%, with a range from 33 to 75%. The polymorphonuclear counts ranged from 1,500 to 7,500 while the lymphocytes ranged from 1,000 to 4,500 (15 to 60% of the total). Various textbooks give ranges from 3,000 to 7,000 (55 to 70%) for polymorphonuclears and 1,200 to 4,000 (20 to 40%) for lymphocytes. Children generally have a lower proportion of polymorphonuclears than adults. Under wartime conditions, a high proportion of healthy working adults may have fewer than 3,000 polymorphonuclears (Britton, C. J. C.: *Lancet* **2**:289, 1943). The above observations support the clinical impression, cited by the inquirer, that many patients have fewer than 60% polymorphonuclears without evidence that this finding is associated with abnormal conditions or a lowered "resistance." There are, however, two reservations to the above statement: 1. Technical factors can alter the apparent differential count (e. g., counting only in the center of a blood smear, where the lymphocytes tend to accumulate). 2. Although "lowered resistance"—insofar as this term has a meaning—will be deduced from a patient's history or physical examination much more definitely than from a differential count, there are conditions associated with neutropenia that should be looked for in cases in which genuine neutropenia exists. Extreme malnutrition, certain types of infection, various types of chronic poisoning, and aplastic diseases are examples. Textbooks on hematology give further specific details on this question.

RELIABILITY OF TUBERCULIN TEST

To the Editor:—*A 30-year-old school teacher had pancarditis following influenza. His temperature spiked to 105 F daily for three weeks. Several weeks later pleural effusion developed that on culture grew two colonies identified as Mycobacterium tuberculosis. Guinea pig inoculation reported granulomatous inflammation with caseation necrosis of the lymph nodes, but no acid-fast organisms were seen. The patient has made a complete recovery with normal heart silhouette, normal electrocardiogram, and normal chest roentgenogram. He has been given 1 gm. of streptomycin twice weekly and 8 gm. of p-aminosalicylic acid daily for six months. The tuberculin skin test (purified protein derivative) is negative in first and second strength. Could you inform me as to the reliability of the tuberculin test when properly performed, in determining the immunological response to tuberculous infection? Does a negative tuberculin test positively rule out the possibility of a previous infection in the recent past?*

Malin B. Shaw, M.D., Covina, Calif.

Answer.—While the symptoms and clinical course of the case described are compatible with a diagnosis of tuberculous pleural effusion, the negative tuberculin test is convincing evidence that tuberculosis is not present. When the issue is so important as in this case, it is recommended that the second strength tuberculin test be repeated to exclude technical errors and, in addition, the test may have been carried out during the interval between the acquisition of the infection and the development of tuberculin allergy. It is believed that from six to eight weeks is required for allergy to develop even though symptoms may appear earlier. Pleural effusion in tuberculosis is thought to be an allergic phenomenon. False positive reports of finding acid-fast bacilli in cultures are encountered occasionally. The identification of Mycobacterium tuberculosis is difficult and should be entrusted only to laboratories that do a volume of such work and are well supervised by experienced physicians.

CORTISONE AND TUBERCULOSIS

To the Editor:—*A patient with active tuberculosis has a severe febrile, generalized mucocutaneous eruption. Would it have been permissible to give him 15 mg. of hydrocortisone, four times a day for five days, in spite of the known untoward effect of cortisone on the course of the tuberculosis?*

Walter Weinberger, M.D., Cresson, Pa.

Answer.—The degree of hazard to tuberculous infection produced by cortisone therapy has not been determined. Most evidence is based on studies in experimental animals, and these indicate clearly that tuberculous infection proceeds more rapidly under the influence of cortisone. Much or all of this adverse effect can be prevented when the antituberculosis drugs are given. The most urgent indications for cortisone therapy should be observed despite tuberculous disease, and antituberculosis drugs, chosen according to the sensitivity of the strains in question, should be administered simultaneously. Cortisone in all forms should be withheld from tuberculous patients when the indications for hormone therapy are not urgent. The incompletely described situation mentioned in the query does not seem to constitute an urgent indication for treatment with hydrocortisone.

SARCOIDOSIS

TO THE EDITOR:—*A 45-year-old man three years ago complained of tiredness, malaise, and loss of appetite. He was checked by an internist for duodenal ulcers. With ulcer treatment, he did not improve. Recently roentgenograms showed duodenal cap deformity. Surgery was advised, and laparotomy was performed by a good surgeon. There was no evidence of ulcer, but the liver and spleen were covered with gray nodular growths. Biopsy was made by a competent pathologist, and a diagnosis of Boeck's sarcoid was made. This man has no skin involvement. I would appreciate information on this type of disease. Is x-ray treatment advisable?* *Lew H. Hauman, M.D., Toledo, Ohio.*

This inquiry was referred to two consultants, whose respective replies follow.—ED.

ANSWER.—The diagnosis of sarcoidosis cannot be established by pathological study alone, inasmuch as an indistinguishable histological appearance can be produced by tuberculosis, histoplasmosis, and berylliosis. These causes of epithelioid tubercles must be excluded and confirmatory evidence of sarcoidosis sought by appropriate laboratory studies. Elevation of the serum globulin level and x-ray evidence of pulmonary infiltration or mediastinal adenopathy would favor the diagnosis of sarcoidosis, as would a negative tuberculin test. Involvement of the liver and spleen is extremely common in sarcoidosis, but lesions elsewhere in the gastrointestinal tract are remarkably rare. Peritoneal tubercles are usually the result of tuberculous peritonitis rather than sarcoidosis. Specific therapy is not available. X-ray therapy has been tried in this disease but has not proved valuable. Cortisone is effective, but it should not be employed if there is any doubt about the diagnosis. Cortisone would be contraindicated in the presence of tuberculosis.

ANSWER.—Sarcoidosis (Boeck's sarcoid), a disease of unknown etiology, produces a reaction in reticuloendothelial tissues characterized by the formation of "hard" tubercles. The disease runs a long course and is characterized by spontaneous remissions. It is rarely fatal, though in many patients with the disease clinical tuberculosis ultimately develops. When tuberculosis develops, the sarcoid lesions tend to disappear. Reviews of the literature on the pathogenesis and clinical picture of the disease may be found in articles by Longcope [1] and Freiman.[2] Involvement of the spleen frequently occurs, and occasionally the spleen may assume tremendous proportions. Involvement of the liver is rarely recognized clinically. Many cases of sarcoid are first recognized when the lesions are found in diagnostic aspiration biopsy specimens of the liver.

X-ray therapy has afforded no conclusively beneficial results. Recent experience with hormone therapy as described by Harvey [3] and others has indicated that the use of corticotropin (ACTH) or cortisone may reduce the host response, cause the local lesions to diminish or disappear, and permit the patient to improve clinically though the disease process itself may not be cured. Care should be taken in the administration of hormone therapy to this patient for two reasons: 1. Corticotropin or cortisone will frequently cause an exacerbation of the symptoms of duodenal ulcer and may precipitate bleeding or perforation. 2. Corticotropin and to a somewhat greater extent cortisone, by reducing tissue reaction, may activate quiescent tuberculosis and induce a symptomatic spread of the disease. A chest roentgenogram should be made before therapy is started and be repeated six weeks and six months after completion of therapy. It is probably wise not to use hormone therapy if the tuberculin skin reaction is known to be positive. Simultaneous administration of streptomycin or other tuberculostatic drugs has not improved the results with hormone therapy.

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POSTMORTEM BLOOD ALCOHOL DETERMINATIONS

TO THE EDITOR:—*A blood alcohol determination was taken from the heart blood of a person who had died several hours prior due to trauma. The body had not been under refrigeration. What changes in blood alcohol level might have occurred from a level present at the time of death? Does such a determination have a legal significance in attempting to determine the presence or absence of alcoholism at the time of death?* *M.D., Georgia.*

ANSWER.—The most commonly used methods for estimating the concentration of alcohol in the blood are relatively nonspecific in that they are sensitive to a variety of volatile reducing substances. In living persons the methods are valid in that it is unlikely that any reducing substances other than alcohol would be present in significant amounts. In cadavers, reducing substances other than alcohol may be formed during putrefaction, thus leading to false positive tests or incorrectly high values. If, in the case in question, the interval between the person's death and obtaining the sample of heart blood was no longer than four hours and if the blood sample was promptly refrigerated or otherwise protected against deterioration, the results of chemical analysis for alcohol were probably valid. If, on reaching the analyst, the sample showed hemolysis or other evidence of bacterial contamination, the results of the test were probably not valid. The legal significance of any determination usually rests with the jury. If the analyst states on examination that he believes that the value reported by him was a close approximation of the antemortem concentration of the blood and if that concentration is high enough in his opinion to account for intoxication, the jury is likely to be disposed to accept these statements as facts.

NONRACHITIC FLATTENING OF SKULL

TO THE EDITOR:—*An 11-month-old baby boy weighed 10½ lb. (4,763 gm.) at birth and appeared normal at that time. At one month of age his head was obviously uneven. The left frontal and right parietal and occipital bones were somewhat depressed. My impression at that time was deformity due to habitually sleeping on one side. I emphasized proper mineral and vitamin intake and prescribed calcium phosphorus, iron, and multivitamin preparations. I also advised having the baby sleep face down, and the mother apparently has followed these instructions. There has been no improvement in the last eight months. The baby walks when holding onto chairs and eats, sleeps, and sits well. His height and weight are in the upper limits of normal. The baby has two normal older sisters. Other bones appear normal, but x-ray studies have not been done. Skull roentgenograms at 5 months showed open frontal and occipital fontanelles. The fontanelles have since closed. Please advise as to the probable diagnosis and treatment.* *M.D., Washington.*

ANSWER.—From the facts stated, the infant is suffering from nonrachitic flattening of the skull. The distortion is only temporary and disappears between the first and second year. In spite of the closure of the fontanelles, the suture lines are open and adjustment will undoubtedly take place.

DANDRUFF

TO THE EDITOR:—*A patient has dandruff that has responded well to selenium sulfide (Selsun). However, the dandruff is becoming heavier. It clears immediately after application but returns in four or five days. Please suggest some alternate type of therapy to clear this patient's scalp.* *John A. Putnam, M.D., Carthage, Mo.*

ANSWER.—All textbooks of dermatology discuss the condition (alopecia seborrheica) fully and list remedies for it. A time-tested one consists of a mixture of 3% salicylic acid and 5% sulphur precipitate in hydrophyllic base. The concentrations may be increased or decreased if necessary, and the ointment should be applied often enough to control the scaling.

LOSS OF TASTE AND SMELL

To the Editor:—*A patient lost the senses of taste and smell completely after trigeminal neuralgia. Is there any treatment that will help?* *Arthur Samuel, M.D., Chenoa, Ill.*

Answer.—Almost invariably the loss of the senses of taste and smell is actually a loss of the sense of smell alone. The ability to differentiate such tastes as salt and sweet is usually retained. However, as both the taste and smell senses are bilateral functions, smell having to do with both sides of the nose and taste having to do with both sides of the tongue, it is impossible to understand how trigeminal neuralgia or an operation for its relief could be responsible for loss of either or both of these sensibilities. Something else must be responsible.

HYPOTENSION IN CARDIAC INFARCTION

To the Editor:—*In answer to a question on "Hypotension in Cardiac Infarction" in* The Journal, *Aug. 15, 1953, page 1583, your consultant makes several statements, with two of which in particular we take exception. He says "So many patients who appear to be in critical hypotension suddenly begin to recover spontaneously." And later, "The use of pressor drugs is not encouraged. They are used, as a rule, only as a last resort and have been found generally ineffective. At best, the result is transient."*

The mortality rate for shock (i. e., critical hypotension) after myocardial infarction is roughly 75 to 90%. Hence, the development of effective means of combating such hypotension is of prime importance. The most effective such agents at present are the pressor drugs, by means of which the mortality has been reduced during the past several years by roughly 50%. This reduction has occurred in patients who were critically ill and in undoubted shock. While it is true that the effect of intermittent injection of certain of these substances, such as phenylephrine (Neo-synephrine) hydrochloride, methoxamine, and mephentermine, is transient, it has been demonstrated repeatedly that the use of arterenol by continuous intravenous drip is associated with a well-maintained pressor response in at least half the patients thus treated. Our usual method of administration is as follows:

Because veins are usually collapsed or may collapse, a polyethylene catheter is inserted into the vein through either a suitable large bore needle or by means of venesection and cannulation; it is then left in place until the patient is either out of shock and in a stable state or he dies in intractable shock or for other cause. An ampul of arterenol (available as Levophed, 4 mg. per ampul) is diluted in 500 or 1,000 cc. of distilled water and is administered by continuous intravenous drip. The rate of flow is set at that necessary to bring and maintain the blood pressure as nearly as possible at a normal level. Frequent blood pressure determinations must be made; this necessitates constant medical and nursing observation. When the patient appears to be out of shock and in a stable state as shown by the need for smaller amounts of arterenol, the drip may be temporarily discontinued. To keep the tubing open for subsequent emergencies, a slow drip of 5% glucose solution is maintained through the opposite arm of a Y tube. The important complications of such therapy are phlebitis and slough, but because of the gravity of the situation, these should not deter from treatment.

A number of patients will not respond to this regimen; there is evidence that cortisone may potentiate the effects of arterenol in these instances. Because of its effects on heart rate and blood pressure in patients with heart block, isopropyl arterenol is of particular importance in block associated with heart block.

Robert W. Oblath, M.D
George C. Griffith, M.D.
University of Southern California School of Medicine
1200 N. State St., Los Angeles 33.

To the Editor:—*In reply to a question regarding the treatment of shock associated with myocardial infarction (Hypotension in Cardiac Infarction, Queries and Minor Notes,* J. A. M. A. **152**:1583 [Aug. 15] 1953) *it was concluded that blood transfusion is the treatment of choice and "the use of pressor drugs is not encouraged." Certain unwarranted statements are also made concerning arterial transfusions.*

There has always been an unfortunate laissez faire attitude concerning the shock state accompanying myocardial infarction. This stems from a fear of "putting a greater load on a damaged myocardium." Obviously, in some cases of shock, there is so much myocardial damage due to coronary occlusion that death supervenes despite all attempts at medical therapy. However, in many cases, the increase in peripheral resistance produced by pressor drugs is followed by dramatic clinical improvement and recovery from the shock state (Miller, A. J., and others: J. A. M. A. **152**:1198 [July 25] 1953).

Pressor drugs such as mephentermine (Wyamine) and levarterenol (Levophed) require no special apparatus for administration, are easily controlled, and are safe in that they do not increase myocardial irritability or overload the heart. They may be given by slow intravenous drip to maintain a sustained blood pressure rise to desirable levels. The primary objective of therapy is to restore the effective head of blood pressure in the aorta in perfusing the coronaries and other vital circulations. Since blood volume is ordinarily not disturbed, blood or plasma transfusion is usually not indicated. The effectiveness of arterial transfusion has yet to be demonstrated (Case, R. B., and others: J. A. M. A. **152**:208 [May 16] 1953); *it is time-consuming, requires special equipment, and has certain inherent dangers.*

If acute congestive failure is present, it must be treated vigorously with rapid-acting digitalis glycosides, positive pressure oxygen, and even phlebotomy. In general, since shock occurs in approximately 10% of all cases of myocardial infarction and carries with it a very high mortality if untreated, it is felt that vigorous early therapy with pressor amines is the treatment of choice.

Bernard L. Brofman, M.D.
Mount Sinai Hospital
1800 E. 105th St., Cleveland.

MARKING THE SKIN BEFORE SURGERY

To the Editor:—*Concerning the query "Marking the Skin Before Surgery" in* The Journal, *Jan. 16, 1954, page 289, brilliant green does not make resistant marks in my experience. About the same result can be achieved by the use of the nonsmudging type of ball-point pens. The best marks are produced with a wetted stick of fused silver nitrate. They withstand any type of preoperative preparation, they contrast well with the red mercurial dyes usually used in surgery, and, though they are persistent, they will have disappeared by the time the patient does not need dressings any longer.*

Hans L. Popper, M.D.
185 N. Wabash Ave., Chicago.

To the Editor:—*In the query that appeared in* The Journal, *Jan. 16, 1954, page 289, Dr. Fitzgerald of Mississippi asked what method or solution may be used to make marks on the skin over varicose veins before surgery that will not disappear with scrubbing? In the* New York State Journal of Medicine (**52**:562, 1952) *was reported a new ink (Cado skin marking ink) to delineate varicose veins. It will not wash off with any solution except ether or benzene. The leg is prepared with pHisohex (pHisodium with 3% hexachlorophene added), alcohol, and tincture of thimerosal (Merthiolate). After operation the ink can be removed with ether or benzene. I have found this ink useful for preoperative marking of varicose veins or any other lesion for which a skin marker is desirable.*

Robert A. Nabatoff, M.D.
1150 Park Ave., New York 28.